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The Peer Review Board encourages contributions to the Journal on all areas of herbalism. Instructions for contributors can be found on the inside back page.

The NHAA was founded in 1920 and is Australia’s only national professional body of medical herbalists.

The Association is a non profit member based association run by a voluntary Board of Directors with the help of interested members. The NHAA is involved with all aspects of medical herbalism.

Our primary role is to support practitioners of herbal medicine through:

• To promote, protect and encourage the study, practice and knowledge of medical herbalism.
• Promote herbal medicine in the community as a safe and effective treatment option.
• Maintain and promote high educational standards for practitioners of herbal medicine.
• Encourage the highest ideals of professionalism and ethical standards for practitioners of herbal medicine.
• Advocate ethical and sustainable methods of growing, harvesting and manufacturing herbal medicines.
• Provide peer support for practitioners and students of herbal medicine.

There are four categories of NHAA membership:

**Full membership**
Practitioners who have undertaken formal studies in the health sciences and the principles and practice of medical herbalism. 
Annual fee $250 and a $30 joining fee.

**Full ATSI membership**
Aboriginal and Torres Strait Islander practitioners who have undertaken formal studies in bush medicine and Western herbal medicine.
Annual fee $60 and a $5 joining fee.

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**Companion membership**
Companies, institutions or individuals involved with some aspect of medical herbalism. 
Annual fee $160 and a $20 joining fee.

**Corporate membership**
Companies, institutions or individuals interested in supporting the NHAA. 
Annual fee $3000.00.

All prices include GST

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‘Spring has sprung’ and I wonder how we got here so fast. New Year feels like yesterday. With spring comes the 10th anniversary of National Herbal Medicine Week with celebrations in Adelaide and Sydney from 19-25 September. Practitioners and the public are most welcome to attend.

The NHAA national seminar series is well underway with presentations well attended and the feedback suggests popular, if not a little controversial for some. Rob Santich and Jerome Sarris are giving lively and interesting presentations. The association aims to present unbiased information to practitioners and students for educational purposes or to encourage wider debate and research. The opinions expressed by presenters do not necessarily reflect the position or policies of the NHAA. The association believes members have the right to hear all sides of any debate and use their skills as researchers to discriminate the ‘truth’ of any matter and how this might apply within their practice.

As always the NHAA is working to gain recognition for the work done by herbalists and naturopaths in promoting and supporting the health of the Australian people. Recently I wrote to each Health Minister across Australia requesting more be done to recognise the contribution of the professions and to protect the public from poorly or untrained practitioners. The responses received so far all appear to have directed the responsibility elsewhere. Even so we continue to request meetings to advance our cause and will keep you all informed.

The NHAA Annual General Meeting is set down for early November in Sydney. I have met many members over the years who would like to be involved but don’t feel they have much to offer as a board member. The only qualifications needed to become a board member are to be a full member of the association, have a passion for herbal medicine and a willingness to give back to your profession. Every new member joining the board brings a new dynamic and enthusiasm. I have presided over seven boards now, every one different. What is always true and consistent is that boards meld together to form a team. Every member ably and professionally supported by the office staff, the company secretaries and volunteers. Each and every person has supported me with high quality services, advancing and growing the association to a new level of professionalism, responsiveness and transparency to our members, the public and governments alike.

There have been many other changes big and small along the way, far too numerous to mention here. These changes were only possible because of the will, enthusiasm and commitment of a group of dedicated volunteers - our board members ably and professionally supported by the truly hard working office staff.

I would like to take this opportunity to publicly say a heartfelt thank you to all board members with whom I have served, the office staff, the company secretaries and the volunteers. Each and every person has supported me unreservedly, both professionally and personally over the years and I thank them all.

The current board is dedicated to providing members with high quality services, advancing and growing the profession. The association remains in good hands.

John Baxter
President
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Mental health, childhood resilience and autism

Rob Santich  *A childhood narrative*  
Delving into some of the forces directed at children in the modern world that can lead to disharmony and loss of resilience, with concepts of treating children with herbal medicines.

Dr Jerome Sarris  *Phytomedicines for psychiatric disorders: old flames and new romances*  
Current evidence for herbal medicines in the treatment of a range of mental health conditions and the potential future use of genetic technologies to tailor herbal treatments.

Rob Santich  *Childhood behavioural disorders*  
The treatment of autism and an update on the persistent controversial link between the MMR vaccine and autism.

Dr Jerome Sarris  *Clinical integrative models to treat mood and anxiety disorders*  
A clinical framework for treating mood and anxiety disorders with differential treatment protocols and prescriptions for depression, bipolar disorder and comorbid anxiety and insomnia.
Monitoring cancer patients for best outcomes

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Presented at the NHAA 7th International Conference on Herbal Medicine in July 2010.

Introduction

Despite enormous amounts of money that are being funnelled into cancer research, both in Australia and in Western countries worldwide, the incidence of cancer is gradually increasing. This research money is predominantly being channelled into gene therapy and pharmaceutical treatments with significantly smaller amounts being utilised for dietary and lifestyle research. Overall:

- One in 3 men and one in 4 women will be diagnosed with cancer before the age of 75 years.
- Annual mortality is 29% of total male deaths, 25% of total female deaths.
- Over the last thirty years incidence has been increasing (except for lung cancer in males).
- The 5 year survival rate for males is 49.5%
- The 5 year survival rate for females is 58.2% for all types of cancer.

With these figures the questions that need to be asked are: is our research money is being allocated effectively; and is 5 years an effective measure for survival time?

Important medical treatments such as Tamoxifen\(^{\text{a}}\) for breast cancer are only prescribed for 5 years as after that the side effects become increasingly risky.

In Australia increasing numbers of people are choosing to utilise alternative treatments when they are diagnosed with cancer. The statistics show that 33-83% of people with cancer choose complementary and alternative medicines (CAM) after they have been diagnosed and commonly alongside medical treatments. The statistics also show that the most common group that utilises these therapies is educated women with breast cancer. In Europe the figures are similar with 48% of people with the diagnosis of cancer using herbal medicines.

Research on why CAM therapies are increasingly being used shows an overwhelming feeling that it increases the patient’s optimism for healing, ie the reason for their choice was the increase of hope (Richardson 2000, Molassiotis 2006).

The philosophy behind the practice

Medical diagnosis and practice is overwhelmingly disease based. This is useful, as accurate diagnosis of disease is important to determine options for treatment, especially in life threatening diseases such as cancer. But in medicine, although the level of treatment success may be associated with the diagnosed disease, it is not good in improving a person’s health. In fact it has so little understanding of health (apart from a person not suffering any obvious symptoms) that while medicine has specific treatments for specific diseases, it has very few interventions based on the improvement of health.

Complementary and alternative medicine, on the other hand, focuses on improving or returning a person to a state of optimal health of which it can measure (and monitor) various parameters. Health is determined by the feeling of vital wellness as well as the prevention of further illness.

These polarised philosophies, concepts and methods of practice both have their place in a true health care (not disease focussed) system and can work in well together providing a much more total approach.

Medical diagnostics and screening

To follow the medical approach of diagnosing and monitoring cancer patients, the following (briefly) are some of the tests utilised.

Ultrasound is a relatively safe procedure and useful diagnostically. Medically it is not commonly recommended for breast screening as it is a more lengthy procedure and may not detect DCIS as readily as a mammogram. However it should be recommended as it is effective and safer.

Colonoscopy can be useful to detect bowel cancer, with minimal side effects depending on the pre-treatment and any reaction to anaesthetic.

Biopsy: core, FNB, excisional (after surgery). Excisional biopsies are the safer method as breaking the capsule (of a potential tumour) to obtain a sample increases its likelihood of spread. This needs to be balanced against the risk of anesthetic if doing a lumpectomy in cases of significant doubt re the nature of the lump (Hansen 2004).

Sentinel node biopsy can be useful to define the affected lymph nodes in regard to spread of the tumour and can prevent unnecessary axillary lymph node clearance, thereby reducing the risk of chronic lymphedema.

Radiation: there are various diagnostic techniques that involve exposure to varying doses of radiation. It needs to be remembered that all radiation is cumulative and there is a finite maximum dose that any individual can receive before risking further illness, such as cancer or significant genetic abnormalities. When utilising radiation in its many forms for diagnosis (and its potential...
for cumulative damage) it is important to weigh up the usefulness and accuracy of the information received for diagnosis, against its potential harm with the cumulative exposure. Many years ago annual chest x-rays were ceased for this reason and today this brings annual or biannual mammograms into question. Frequent CT (or CAT) scans are also under the spotlight.

- Mammograms have cumulative radiation issues. A review conducted by the Cochrane Collaboration concluded that it was possible that mammograms caused more harm than good. It showed that it possibly reduced mortality by 15% (a risk decrease of 0.05%), but led to 30% overdiagnosis and overtreatment (a risk increase of 0.5%) (Gotzsche 2006).
- X-rays have cumulative radiation issues. Whole body scans are potentially a problem, especially as ‘health check-ups’ when there is no specific indication for the procedure.
- Bone scans involve a low amount of radiation and are diagnostically useful for the detection of bony metastases.
- CT (computerised tomography) also called CAT (computerised axial tomography) scans show organs, tissues and any abnormality. Contrast dyes are sometimes used. However CT scans involve comparatively high radiation levels and should only be used when absolutely necessary. Spiral CT scans take 3-D pictures of the body but involve more radiation as the whole body is irradiated.
- PET (positron emission tomography) scans are most effective for large and aggressive tumours but not as useful in the early stages. A small radioactive tracer is attached to a sugar and injected and imaged so the radiation received is much lower than that of CT scans. PET scans show metabolic activity and cancer cells are usually more active than normal cells. They are however more expensive.
- MRI (magnetic resonance imaging). The person is placed in a magnetic field and useful diagnostic imaging is obtained. MRI scans give diagnostically useful and detailed images. The long term risk has not been researched sufficiently and is therefore unknown.

Cancer markers of blood, urine and tissue are not ideal but are used for four main reasons:

a) Screening a healthy population or high risk population for cancer
b) Diagnosing cancer
c) Determining prognosis
d) Monitoring patients while in remission or while undergoing treatment.

Tumour antigens are useful markers but not specific for cancer and can indicate many other diseases, particularly inflammatory conditions. Examples are:

- CEA (carcinoembryonic antigen, normal <2.5ng/mL) can be useful in recurring tumours as it can indicate clinical relapse by several months. It is primarily used in colon cancer but can also be useful in cancer of the breast, lung, pancreas, stomach and ovary.
- AFP (alpha feto protein) is a fetal serum glycoprotein which shows up in various cancers especially hepatocellular cancers, but also in normal pregnancies.
- CA 125 is defined by a monoclonal antibody and is an antigen present on 80% of nonmucinous ovarian tumours
- CA 19-9 in a monoclonal antibody useful to detect gastrointestinal adenocarcinomas.
- PSA (prostate specific antigen) is a glycoprotein marker produced either by the body in the presence of a tumour or by the tumour itself (normal 0-4 ng/mL). While a useful indicator, it is not cancer specific but prostate specific, detecting abnormalities of the prostate that can include enlargement or the process of aging. There are racial differences, Asian men having lowest levels.

Immunoglobulins (paraproteins, antibody molecules) if raised are indicative of multiple myeloma.

Hormone receptors positive or negative (from biopsy). Whether a tumour is estrogen or progesterone positive or negative can determine the treatment offered both medically and with complementary medicine so is important as a diagnostic tool. Apart from breast cancer, other tumours that may be estrogen receptor positive include prostate cancer, bowel cancer, melanoma and some lung cancers. High levels of urinary 16 alpha hydroxyestrone has promise as a useful marker for breast cancer in post menopausal women (Kabat 1997) and in prostate cancer (Barba 2009). Hormones are also produced by islet cell tumours (insulin), medullary thyroid carcinoma (calcitonin). Some lung cancers increase the levels of the hormones ACTH (adrenocorticotropic hormone) and ADH (antidiuretic hormone).

Genetic markers HER-2, BRCA1 and 2. These tumour suppressor genes are called breast cancer type 1 (and 2) susceptibility proteins. They are produced in the body to assist in the repair of damaged DNA (Wang 2000). There is some doubt about the usefulness of these markers as evidence indicates that less than 5% of cancer is genetic, and there is increasing evidence to show that the environmental impact is in fact much more of a risk factor. There is a field of science called epigenetics that researches the environmental evidence for diseases, including cancer (Kling 2003, Jones 2001, Seppa 2000).

Gene testing. There is research being conducted world wide on specific genes that code for specific nutrients. Kits to test these will soon be available in Australia and will specify individual (genetic) requirements for nutrients. It is an emerging and exciting field for complementary medicine practitioners.

Tumour grading is a microscopic classification of cancer cells and how quickly they are likely to grow.
Tumour staging (stages 1-4) has several elements based upon the extent of the tumour and the degree of spread. These elements are:

- Location of the primary tumour
- Tumour size and the number of tumours
- Lymph node involvement
- Cell type and how closely the cancer cells resemble normal tissue
- Presence or absence of metastasis

Tamoxifen screening has become available and is a measure of selected CYP 450 pathways in the liver. This test will ascertain whether tamoxifen, if prescribed, will be effective or not. It does not come under Medicare at this stage and is very expensive (Rae 2009).

What we need to consider with the wide range of tests available is that generally these markers do not diagnose the disease (such as cancer) but give a measure of possibilities for the risk of a specific disease and (if abnormal) lead to further testing. With medical testing the value of the diagnosis has to be weighed against the potential risks of the procedure compared with the diagnostic information obtained.

Questions to be asked before making decisions re testing and the potential treatment that will be recommended from the results obtained:

- Do these tests provide useful information?
- Are there safer alternatives?
- What value is the diagnosis/screening? Does it provide information for decision making about treatments from both the patient and practitioner perspective?

Medical diagnosis can be useful for practitioners but what does the diagnosis of disease tell you about the person’s health, or about the possible causes of the problem? Practitioners need effective ways of measuring the parameters of health (or otherwise) that they can then manipulate with the modalities they utilise.

Diagnostic testing that is useful for CAM and integrative practitioners

Tests must be easy to access, relatively non invasive and provide information that the practitioner and patient can use. This will allow both practitioner and patient:

- to determine the most appropriate treatment
- to monitor the progress of patient’s health (and the correction thereof)
- to monitor the effectiveness of chosen interventions
- be relatively inexpensive (rarely funded by Medicare)

Medical blood testing that I find useful in my practice and that is not cancer specific:

- Homocysteine (sulphation pathway activity).
- ESR, CRP (measures of inflammation)
- FBC (WCC – Neutrophils, Lymphocytes can indicate infection)
- Iron stores
- LFTs (liver function tests)
- TFTs (thyroid function tests)
- Electrolytes
- Hormone studies including salivary hormone testing:
  - DHEA, cortisol (adrenal)
  - Vitamin D etc.

These can be indicators for nutritional and herbal interventions and can correlate with other testing such as LBA/CRT (see below).

What would be the perfect test?

The perfect test should be:

- Accurate
- Discriminating
- Pain free
- Risk free
- Useful for the modalities utilised by the practitioner (whether in health improvement or in disease states)
- Able to be understood by the patient so they can become involved in the process of healing.

A case study demonstrating the use of CAM testing

In this paper I will present a case study that briefly demonstrates how I monitor the health of my patients to:

- provide a baseline measurement of functional health
- assist in decision making re possible interventions based on these tests
- monitor the progress of the patient (and efficacy of the interventions) over time.

Generally I use Australian Biologics Testing Services for diagnosis and monitoring of the patient. I also use Great Smokies and/or Bioscreen testing services when necessary. In the future I will be utilising the services of Genecare when its services become available.

The tests that I utilise most frequently are:

Live blood analysis (LBA). This indicates various anemias, EFAs, digestive function, immune status and white cell count (WCC), and can detect various organisms including cell wall deficient organisms.

Bolen’s clot retraction test (CRT). Studies show 95% sensitivity and specificity in neoplasm detection. Change is seen often months prior to change in routine pathology. The CRT measures oxidative markers, inflammatory, endocrine, (including adrenal), lymphatic, immune, nutrients such as magnesium, selenium, heavy metals, and vitamin C (Deegan 1997, Wassertheurer 2006, Brzecki 1989)

Contact regulation thermography or thermal imaging

- Thermal scanning is a low invasive, non compressive measurement of specific points on the body measuring regulative ability.
- Thermal imaging gives a coloured picture of the area.

Both of these tests are based on measuring variations to the vascular supply of the skin which then may indicate chronic illness. They can both be used for breast screening prior to ultrasound.
Other tests include lymphatic viability, chemical sensitivity, hair analysis for minerals and heavy metals, food and inhalant allergens, Candida antibodies, salivary hormones, fecal microbiology, phase 1 and 2 liver detoxification pathways and when available gene profiles for specific nutrient supplementation.

**Nested PCR.** This test can use blood or tissue and tests for a variety of pathogenic organisms. It amplifies a few copies of DNA and generates thousands to millions of copies of the particular DNA sequence. It is very useful for detection of chronic illness potentially stimulated by organisms such as Mycoplasma, Chlamydia, Borrelia etc.

### Statistics for infection and oncogenesis

In 1996 the World Health Organisation estimated that up to 84% of cases of some cancers are attributable to viruses, bacteria and parasites. In developed countries approximately 8% of malignancies have infection as a cause; in undeveloped countries up to 23% of malignancies are due to infectious agents. The most common pathogens causing problems are Helicobacter pylori, hepatitis B and C, Epstein-Barr virus (EBV), human papillomavirus (HPV), and possibly cell wall deficient (CWD) organisms (these include mutated forms of Candida albicans). There is evidence to suggest that forms of Mycoplasma have the ability to trigger oncogenesis (Huang 2006), however infection is rarely tested for so in reality the figure may be much higher.

### Case study: diagnosis of pancreatic cancer

I have chosen this case study for several reasons. Pancreatic cancer is a type of cancer that:

- medicine has little to offer in way of treatment (and treatments that were offered were refused by the patient because of the potentially poor outcomes and serious side effects);
- the patient has been monitoring his progress in detail for some time and he is showing improvement utilising herbal and nutritional modalities;
- the negatives are that he has been trying to follow more than one practitioner and has changed his treatment (including herb mix) according to his concerns (and family pressure) at the time. Therefore most of the herbal treatments recommended here have been given inadequate time to work effectively.

In June 2008 the patient went to his doctor with severe digestive symptoms and acute right sided pain. Tests showed a biliary obstruction so he was referred to the hospital where a CT/CAT scan indicated a mass in the head of the pancreas. He decided against surgery at this stage because of the potential risks associated with the procedure.

On his own volition he commenced eating a vegetarian diet, he organised intravenous vitamin C with a local GP who also prescribed Creon (pancreatic enzymes). He then consulted with a herbalist who prescribed MMS, Ribrax (Ganoderma) and a herb mixture, the contents of which he would not divulge to the patient. His digestive symptoms improved and the medical team were adopting a ‘watchful waiting’ approach. He was very interested in his own progress and had regular checkups by his medical team. He was being monitored regularly for blood profiles and cancer markers. He took the herbal mixture on and off over a year.

In September 2009. A repeat CT scan showed that the pancreas was atrophic and that the mass had regressed. On further testing they also discovered a raised IgG4, which is more common in autoimmune pancreatitis. At this time his symptoms were deteriorating and he was experiencing severe reflux and diarrhea. He was further tested with another CT scan which showed duodenal obstruction. A biopsy was conducted on the area of the obstruction with the result that showed a lymphoplasmacytic infiltrate that was positive for IgG4.

In January 2010, due to a recurrence of severe abdominal pain and reflux, and the rise in CRP (C-reactive protein), he was prescribed Prednisolone 45 mg and Pariet. The Pariet gave him minor symptom improvement. Because this condition is so closely associated with the pancreas, diabetes is common and these medications exacerbated his abnormal blood sugar readings. He was therefore prescribed Diamicron 2/day.

April 2010. The patient had continuing duodenal

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**Table 1: Mycoplasma infection in carcinoma tissues** (Huang 2006)

<table>
<thead>
<tr>
<th>Type of carcinoma</th>
<th>Total number of cases</th>
<th>Negative cases</th>
<th>Positive cases (+)</th>
<th>Positive cases (++) (strong)</th>
<th>Total positive cases</th>
<th>Ratio of positive in % age</th>
</tr>
</thead>
<tbody>
<tr>
<td>Esophagus</td>
<td>53</td>
<td>26</td>
<td>21</td>
<td>6</td>
<td>27</td>
<td>50.9</td>
</tr>
<tr>
<td>Lung</td>
<td>59</td>
<td>28</td>
<td>23</td>
<td>8</td>
<td>31</td>
<td>52.6</td>
</tr>
<tr>
<td>Breast</td>
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<td>38</td>
<td>17</td>
<td>8</td>
<td>25</td>
<td>38.7</td>
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<tr>
<td>Glioma</td>
<td>91</td>
<td>53</td>
<td>27</td>
<td>11</td>
<td>38</td>
<td>41.0</td>
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<tr>
<td>Total</td>
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<td>145</td>
<td>88</td>
<td>33</td>
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<tr>
<td>Colon</td>
<td>58</td>
<td>26</td>
<td>19</td>
<td>13</td>
<td>32</td>
<td>55</td>
</tr>
<tr>
<td>Gastric</td>
<td>90</td>
<td>40</td>
<td></td>
<td></td>
<td></td>
<td>56</td>
</tr>
</tbody>
</table>
obstruction, so another biopsy was conducted which showed an invasive adenocarcinoma of the duodenal bulb (possibly of pancreatic origin). To relieve the symptoms a stent was placed in the duodenum. This significantly relieved the pain and improved his quality of life.

On 27 April 2010 he attended the clinic for a consultation, referred by his GP who was concerned that the previous herbal treatments were no longer effective. He also realised he was reacting to Prednisolone, it had induced adrenal dysfunction, so he stopped taking it. He was also taking Paracetamol for pain relief.

On 27 April 2010 he was prescribed:
- Organic Triphala powder 1 teaspoon three times daily in water or juice. Triphala is an ancient Ayurvedic formula that contains Emblica officinalis, Terminalia chebula and Terminalia bellirica and has interesting research regarding pancreatic cancer (Shi 2008).
- Quercetin and bromelain 2 twice daily (as Paracetamol alternative).
- Coriander pesto (for possible mercury toxicity). He recently had all amalgams removed and had not been endo detoxified correctly. Dose of one tablespoon with food daily.
- Selenosol 10 drops twice daily (200 mcg/day.) Super selenium complex (USA) was recommended.
- The MMS was stopped on advice. This is a useful remedy as an antimicrobial but long term use is contraindicated. It may have been MMS that initially reduced the tumour if it had an infective cause. At this stage it was not appropriate to recommend blood PCR (polymerase chain reaction) as the treatment would have significantly obscured the picture.
- The herbal mixture prescribed was based on symptoms and the results of medical testing and was designed to improve parameters in immune, anti-inflammatory, antioxidant, liver and adrenal support, antifungal and digestive systems. The formula contained Andrographis paniculata, Scutellaria baicalensis, Silybum marianum, Tabebuia impetiginosa, Filipendula ulmaria, Rhodiola rosea, Withania somnifera, Eleuthroccoccus senticosis, Arctium lappa and Curcuma longa. Dose 5 mL twice daily
- CRT and LBA were recommended for monitoring.

The patient collapsed the next day after leaving clinic with a possible infection but improved dramatically after 4 days taking the herbs.

Medical

A CT scan on 11 May 2010 showed that the gastric distension had been resolved with stents, the pancreatic duct dilatation had increased with atrophic changes in the body and tail, but the head of the pancreas looked normal. Enlarged retroperitoneal lymph nodes were shown, leading to the possibility of a cystic neoplasm of the pancreas. There was no obvious vascular invasion to suggest an aggressive lesion. A small amount of ascites was observed. There was no significant mass/lesion seen in the head of the pancreas. Conclusion was possible malignant ascites or pancreatitis.

On 14 May 2010 a slightly different herb mix was prescribed according to the LBA and CRT which (amongst other abnormalities) showed significantly abnormal iron parameters and acute infection. The herbs prescribed were Urtica dioica, Phytolacca decandra, Rehmannia glutinosa, Glycyrrhiza glabra, Artemesia annua, Andrographis paniculata, Filipendula ulmaria, Echinacea purpurea, Tabebuia impetiginosa and Arctium lappa.

It would be useful to conduct a PCR on lymphoid tissues or any residual tumour to see what possible infection is still active, but this would involve a more invasive procedure that may be counterproductive at this stage. Vitamin D and homocysteine testing was requested.

Results

CRT and LBA results can be seen in Table 2. These show improvements in CRT: inflammation, oxidation (staging), lymphatics, pancreas, heart, selenium levels and heavy metals; LBA: liver, leukocyte levels and protein digestion.

To date the client is doing well, but has times of regression. He is taking different herb mixtures prescribed by myself and by his previous herbalist as his initial prescription was effective. However this prescription no longer seems to be as effective. By following different regimes it is difficult to determine exactly what is working. He has been advised to stick with a single regime for a period of three months and then repeat the LBA/CRT and medical testing in the same week.

Points to ponder when treating cancer patients overall

From my experience:
- As many patients on chemotherapy have difficulty tolerating alcohol, infusions, decoctions and glyceretachs may be better herbal options.
- Tablets and capsules can be useful but it is difficult getting the formulae required.
- In liver metastases or liver dysfunction always start with low dose herbs and/or nutrients and increase if no reaction. It is relatively easy to over stimulate the liver, raise LFTs and exacerbate symptoms with herbal medicines and vitamin supplementation.
- HER +ve. If a person is prescribed Herceptin, supplement with Co-enzyme Q10 and Crataegus to support the cardiovascular system
- Iscador may be considered as an alternative treatment in breast cancer (Ziegler 2008).

Notes on nutrients and relationships
- Selenium: selenomethionine or selenium yeast is preferred. In the USA you can purchase S-methylselenocysteine and seleno-glutathione.
Results are improved with these but they are illegal to sell in Australia. However patients can bring in enough for their own use (Micke 2009). The available selenium dose in Australia has increased in the last few years and selenomethionine supplementation has been shown to improve deficiency. Dose 400 mcg/day if low.

- Selenium should be taken with methylation factors, folic acid B6 (pyridoxal-5-phosphate is the preferred form) and B12.
- Essential fatty acids and all fat soluble nutrients (such as Vitamins A, D, E and Co-enzyme Q10) should be taken with lecithin to ensure digestion and absorption.
- Vitamin C is better as mixed ascorbates.
- Essential fatty acids and all fat soluble nutrients (such as Vitamins A, D, E and Co-enzyme Q10) should be taken with lecithin to ensure digestion and absorption.
- Bone pain may be alleviated with calcium orotate.
- If the patient is estrogen receptor positive, think indoles and melatonin. Both of these can be taken with selenium dose in Australia has increased in the last few years and selenomethionine supplementation has been shown to improve deficiency. Dose 400 mcg/day if low.
- There is evidence that an underlying infection of Mycoplasma fermentans (and possibly other cell wall deficient organisms) may trigger oncogenesis. Nested PCR can determine if suspected infection. If so add antimicrobial herbs to the formula.
- Use Forbiotic if on antibiotics (including chemotherapy) as it reduces the gut reaction.

**Conclusion**

Meditation (of any effective form), cancer support groups, counselling and lifestyle changes are all critical components of an effective program.

As long as the patient is monitored closely with both medical and complementary medical techniques and treated appropriately, you can make a difference.

**References**


Table 3: Case study chart of medical testing

<table>
<thead>
<tr>
<th>Date</th>
<th>CA 19.9</th>
<th>CRP</th>
<th>Comments and other tests</th>
</tr>
</thead>
<tbody>
<tr>
<td>28/7/08</td>
<td>2071</td>
<td>6.2</td>
<td>CRP N = 0.5 mg/l</td>
</tr>
<tr>
<td>17/11/08</td>
<td></td>
<td></td>
<td>Ultrasound - 10% tumour shrinkage. Started MMS 02/09 (Feb)</td>
</tr>
<tr>
<td>30/04/09</td>
<td>2022</td>
<td>1.5</td>
<td></td>
</tr>
<tr>
<td>19/06/09</td>
<td>1489</td>
<td>220.8</td>
<td></td>
</tr>
<tr>
<td>17/08/09</td>
<td>1184</td>
<td>14.8</td>
<td></td>
</tr>
<tr>
<td>15/09/09</td>
<td></td>
<td></td>
<td>Pancreatic mass not visible. GIT symptoms for 3/52</td>
</tr>
<tr>
<td>25/11/09</td>
<td>1998</td>
<td>2.8</td>
<td></td>
</tr>
<tr>
<td>4/12/09</td>
<td>2276</td>
<td></td>
<td>IgG4 = 3.864 (N = 0.3 – 2.1)</td>
</tr>
<tr>
<td>15/01/10</td>
<td>2052</td>
<td>11.3</td>
<td>IgG4 = 4.734. Started Prednisolone</td>
</tr>
<tr>
<td>15/02/10</td>
<td>4158</td>
<td>2.1</td>
<td></td>
</tr>
<tr>
<td>18/03/10</td>
<td>4371</td>
<td>12.9</td>
<td>IgG4 2.639. Neutrophils 10.32 (N=2.0-7.5). Lymphocytes 0.78 (N=1.0-4.0)</td>
</tr>
<tr>
<td>20/04/10</td>
<td></td>
<td></td>
<td>HbAlc 7.9 (N= 4.0-6.0) suboptimal</td>
</tr>
<tr>
<td>22/04/10</td>
<td>4570</td>
<td>11.1</td>
<td>Stopped Prednisolone. Paracetamol x 1/day</td>
</tr>
<tr>
<td>30/04/10</td>
<td></td>
<td></td>
<td>Started Triphala, herb mix, quercetin, selenium. Stopped MMS</td>
</tr>
<tr>
<td>12/05/10</td>
<td>2941</td>
<td>135.0</td>
<td>IgG4 2.677. Neutrophils 14.4, lymphocytes =N, Glu 12.5. Fe studies grossly abnormal. Iron, transferrin, TIBC and saturation very low. Ferritin 312 high (N=30-300). LFTs = N Chol 3.0 (L)</td>
</tr>
<tr>
<td>28/05/10</td>
<td>1900</td>
<td>116.2</td>
<td>Feels very well, energy good. 2nd herb mix big improvement</td>
</tr>
<tr>
<td>14/06/10</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>20/07/10</td>
<td></td>
<td></td>
<td>Ascites clearing, feels good (little tired), Neutrophils 7.2.</td>
</tr>
<tr>
<td>11/08/10</td>
<td>4725</td>
<td>21</td>
<td>Been taking herb mixture from other herbalist for 3 weeks. Finding it difficult to take Triphala as dislikes the taste.</td>
</tr>
</tbody>
</table>


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Whole system research of naturopathy and medical herbalism for improving mood and reducing anxiety

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While research on complementary medicine products is on the rise, study of the real life practice and outcomes of naturopathy and medical herbalism is nascent, thus exploration of the effectiveness and safety of this system of medicine is urgently required. This paper explores considerations of whole system research of naturopathic practice, discussing challenges and strengths of this method and provides advice on pursuing this type of research. An example of a current study underway is presented: The Naturopathic Medicine for Improving Mood and Reducing Anxiety Study. The Australian 16 week observational study of naturopathy for treating depressed mood or anxiety has an aspirational goal to collect data over an 18 month period from over 200 client participants (aged 18-70) with either ongoing depression and/or anxiety. Mental health disorders such as depression and anxiety are prevalent and socioeconomically destructive conditions that represent a major treatment focus for clinicians, thus research of this area is vital. The use of a whole system research design to evaluate the efficacy and safety of naturopathic medicine as it is actually practiced will provide benefit to both the profession and the public by potentially validating its therapeutic benefits. Naturalistic pilot studies, such as the one detailed above, provide a platform for future larger scale research using a rigorous controlled design.

Key words: whole system research, naturopathy, herbal medicine, complementary medicine, depression, anxiety, protocol

Whole system research of naturopathy and medical herbalism

Clinical trials using isolated herbal or nutritional compounds have been increasingly conducted over recent years, however study of the actual practice of naturopathy or medical herbalism has surprisingly only recently been explored in three treatment studies. These trials involved the treatment of temporomandibular disorders (Ritenbaugh 2008), anxiety (Cooley 2009) and multiple sclerosis (Shinto 2008).

Randomised controlled trials (RCTs) using isolated components are often regarded as the gold standard measure to determine evidence of efficacy (Verhoef 2007). However many caveats exist when applying a reductive model to determine efficacy of complementary and alternative medicine (CAM) naturalistic practice. CAM practitioners often use individualised prescriptions to treat the ‘whole’ person (not just the symptoms) and this holistic practice cannot be adequately assessed via RCTs that reduce a complex intervention into a single reductive component.

The methodological construct of whole system research has previously been proposed, to meet the shortcomings of reductive research and to better evaluate and understand CAM practice (Kavanagh 2009). This individualised research approach can be applied to naturalistic practice to collect data from multiple samples (or cases studies), or can be applied within a controlled design comparing the outcomes of practice to usual care, standard conventional care or other CAM modalities. Observational naturalistic studies are subject to the methodological limitation of being uncontrolled (having the confound of natural recovery, the ‘black box’ conundrum of not knowing which component/s worked and potential placebo effects) (Herman 2006). Furthermore these studies are confounded by the level of the practitioner’s skill or other individual characteristics.

Regardless, potential advantages in the naturalistic whole system research approach exist. Firstly while we may not know which intervention/s of the treatment worked, we can assess the actual outcome of being treated by a CAM practitioner. The combination of treatments prescribed in addition to usual psychosocial education and the effect of a therapeutic relationship aiming to restore vitality, balance and wellbeing, may be ‘synergistically’ more effective than isolated interventions. Ultimately the study of an isolated natural product or intervention is far removed from the human experience of being treated by a CAM practitioner.

Challenges do however exist when conducting whole system research in the area of CAM. Zick and colleagues (2009) outline five challenges when scientifically evaluating herbal medicine practice: 1) Defining what is ‘herbalism’ and the acknowledgment of differing levels of education and way of practice; 2) the role of industry in potential influencing outcomes; 3) the difficulty in
designing non active matching placebos; 4) quantifying some herbalists’ belief in energetics and a spiritual connection to plants; and 5) designing controlled studies using individualised multi component herbal medicine prescriptions.

To combat these challenges in herbal medicine whole system research, a large cohort of practitioners is required. This way it is possible to compare sub samples of outcomes from practitioners who have differing education levels and who provide differing treatments. Industry can potentially be kept at arm’s length by government funding of research or via funding acquired from unbiased benefactors. A biologically non active pungent plant medicine can be used as a placebo (however any herbal medicines with a remnant bitter or aromatic principle may still have an effect). Energetic aspects and individual beliefs can be explored via qualitative research. The black box issue concerning studies that use multiple herbal components can be ‘unpacked’ by comparing results of different herbal combinations after the study is completed, by studying predetermined combinations via a treatment decision tree (e.g. if a patient presents with X pattern of X condition then prescribe X), or by undertaking the research in a stepped manner (exploring the comparative effects of a single herb versus additional added herbs). Conducting a study using this last approach is however very expensive.

**Naturopathic whole system research of mental disorders**

Mental health disorders, and in particular depression and anxiety, are a major treatment area for practitioners (Adams 2011). Symptoms of clinical depression include low mood or loss of pleasure, symptoms such as feelings of guilt or worthlessness, sleep disturbance, changes in appetite/libido and negative or suicidal thoughts (American Psychiatric Association 2000). Symptoms of anxiety include chronic worry or feelings of being stressed or anxious; symptoms such as heart palpitations, feelings of fear (American Psychiatric Association 2000). Herbal medicine is widely used by individuals with mental health conditions, with United States data from the National Comorbidity Survey Replication (2002) finding that people with mental disorders were significantly more likely to have used herbal medicines for their mental health than respondents who did not meet criteria for a mental disorder (Ravven 2011).

General complementary therapies and medicines are also used prevalently by people with depression or anxiety. United States data from a nationally representative sample of 2055 people interviewed during 1997-1998 revealed that 57% of those with anxiety attacks and 54% of those with severe depression reported using some CAM during the previous 12 months (Kessler 2001). Twenty percent of the sample with anxiety and 19% of those with severe depression visited a CAM practitioner for treatment during the year.

Naturopathic practice in treating depression and anxiety is often based on a biopsychosocial model which views the causation of depression as being multifactorial, with many interrelated influences considered to be involved in a depressive disorder (Sarris 2011). The biopsychosocial model suits the CAM paradigm which treats people from a ‘whole system’ approach, regarding all biological systems as interrelated and fluidic, and views disease causation as being profoundly influenced by a complex array of factors (Di Stefano 2006, Sarris 2010).

The therapeutic application of naturopathic medicine, which uses an integrative biopsychosocial model (ideally with evidence based interventions), may potentially achieve better outcomes than has been shown in studies which have tested individual monotherapies. As reflected in CAM practice, a variety of individualised interventions is commonly used in an integrative manner to treat mental health disorders (Sarris 2010). While individual interventions may have evidence as monotherapies, combinations of treatments used in a ‘person centred’ integrated manner addressing the causes of mental ill health may potentially be more effective by addressing a range of determinants to mental ill health.

As the evidence indicates, depression (and by extension anxiety) are commonly inadequately treated (Rush 2007), with drug therapy achieving first treatment remission in approximately only one third of patients (Hierholzer 2006). Furthermore as a recent review by Fournier et al (2010) in JAMA details, current evidence reveals that synthetic antidepressants are weakly efficacious against depressive symptoms in persons with milder forms of depression. Due to this the conventional idea of ‘giving a pill’ to treat psychiatric disorders can be viewed as antiquated and the study and application of integrated, individualised, whole person care may provide a critical step forward in the field of mental health.

The study of integrative healing systems such as naturopathy, ideally incorporating evidence based interventions, may provide advantages in the treatment of non severe forms of depression and anxiety over conventional pharmaceutical drugs which may cause side effects and appear to have at best moderate efficacy in mild to moderate depression. As the causation/s of depression and anxiety can be viewed as multifactorial (Molina 1983), individualised naturopathic care which treats people with both biological and psychosocial consideration may provide benefits beyond standard care.

To appropriately assess the effects of whole system research of naturopathic practice, mixed method designs can be implemented using a combination of qualitative and quantitative assessments (Verhoef 2007). The strength of combining these methodological approaches includes the ability to assess efficacy (via quantitative outcomes) as well as exploring the healing experience.
group scores were significant. This may provide evidence that the qualitative experiences of participants reflect the numerical quantitative data and/or may provide evidence of unique effects found from naturopathic treatment (and in some cases previously unknown safety considerations).

Currently only one study has attempted to explore the effectiveness of naturopathy for the treatment of a psychiatric disorder. In a Canadian study conducted by Cooley et al (2009), employed adults with moderate to severe anxiety of longer than 6 weeks duration were randomised to receive naturopathic care (NC) (n=41) or standardised psychotherapy intervention (PT) (n=40) over a period of 12 weeks. Participants in the NC group received a range of interventions including dietary counselling, deep breathing relaxation techniques, a standard multivitamin, and *Withania somnifera* (600 mg per day of standardised root). The PT intervention received psychotherapy, matched deep breathing relaxation techniques and placebo tablets.

Of the 75 participants who received eight weeks or more of treatment, anxiety scores on the Beck Anxiety Inventory (BAI) decreased by 56.5% (p<0.0001) in the NC group and 30.5% (p=0.0001) in the PT group. BAI group scores were significantly decreased in the NC group compared with the PT group (p=0.003). Significant differences between groups were also observed on the outcomes of fatigue, mental health, concentration, social functioning, perceived vitality and overall quality of life, with the NC group exhibiting greater clinical benefit. No serious adverse reactions were observed from naturopathic treatment.

While this study reveals encouraging results for naturopathic medicine for anxiety, it should be noted that the study was not naturalistic and thus does not reflect true individualised prescription and practice. Thus there is a further significant need to investigate naturalistic naturopathic practice and to explore this in the critical area of mental health, a common clinical focus of naturopaths.

Depression and anxiety are personally and socioeconomically destructive (Wittchen 2002) and as discussed above a significant percentage of Australians seek CAM healthcare to treat these conditions (Sarris 2010, Bensoussan 2004). However to date little hard evidence exists chronicling prescriptive practices of this field and no studies have used validated assessment tools to examine the efficacy and safety of naturopathy and medical herbalism naturalistic practice in the treatment of depression and anxiety. Due to this research is vital to address this gap in the field for the betterment of the profession and for the potential benefit of sufferers of depression and anxiety.

**Whole system research in action**

Born from the current deficit of practitioner centred studies using a whole system research model, the Naturopathic Medicine for Improving Mood and Reducing Anxiety Study was created. The project aims to explore the efficacy and safety outcomes of naturalistic naturopathic treatment of people with depression or anxiety. The combined outcomes of depression and anxiety were chosen for this study as these are common mental disorders that often occur comorbidly (Kessler 2008). The observational study has an aspirational aim to collect data from over 200 participants within 18 months. The primary aims of the study are to evaluate the efficacy and safety of Australian naturopathy and medical herbalism on the outcome of depressed mood and anxiety, assess which interventions are being prescribed and to explore clients’ experiences of being treated by a naturopath.

The study will be managed from The University of Melbourne at The Melbourne Clinic (Richmond), and data will be collected from naturopaths throughout Australia (in private practice and from private colleges in Brisbane and Melbourne). The project will run from August 2011 to November 2012. The study has ethical clearance from The Melbourne Clinic Research Ethics Committee (ID 196) and is registered on The Australian and New Zealand Clinical Trials Registry (ID ACTRN12611000756921).

Any persons aged 18-70 years presenting with depressed mood and/or anxiety (ongoing for more than 2 weeks) as their primary complaint and reason for treatment (although they can have other health issues) are eligible for inclusion. Due to the naturalistic observational design, the only exclusion criterion is that participants must have competent English skills and be able to understand and fill out the assessment forms. Data collection will occur during week 0 (first visit baseline) and at time points over 16 weeks as following the naturalistic naturopath/client treatment process. The purpose is to keep data collecting achievable so as to minimise drop outs and any negative impact on the therapeutic relationship and time requirement.

Treatment effects will be assessed via validated forms: Profile of Mood States form (POMS); Depression Anxiety Stress Scale (DASS); and the General Health Questionnaire (GHQ-28). Side effects and participant experiences are to be explored via a qualitative assessment form. Naturopaths will fill out a purpose designed form to chart their prescription. Data from the completed information forms are sent to The University of Melbourne (Department of Psychiatry at The Melbourne Clinic) for analysis.

Limitations to this whole system research design are acknowledged. Firstly these types of studies are not controlled (i.e. not compared with a placebo intervention or positive control such as standard care), and it is likely in the case of the study detailed above that over time the client’s depression and anxiety symptoms will improve. Due to this it is not known whether this effect would occur from naturopathic treatment or would have happened naturally over time. If however the results on the validated outcome scales revealed a significant
effect over time that is comparable with other studies using validated treatments (such as antidepressants or cognitive behavioural therapy), then this would hold confidence in its effectiveness. Furthermore qualitative assessment may reveal key themes of personal benefits from the treatment.

Another limitation is that the study is designed to collect data up to 16 weeks. In some cases the effects of the prescription and lifestyle adjustments may take many months to take full effect. Regardless, if little or no effect has occurred after four months of treatment, it is unlikely that the client will return to the practitioner for continued treatment. A final limitation acknowledged is that there will be marked variations of practitioner education levels and the treatments they provide. If the sample size is large enough these differences can be teased out during data analysis to determine which covariate factors affect the outcomes. For example it is possible to determine which herbal medicine formulation or treatment combinations were more effective and whether more experienced clinicians had better results.

The results from such a pilot study could be used to apply for a grant to fund a much larger controlled study of naturopathy in the treatment of depression. A future study with a more robust methodological design would seek to study a clinical sample of people with DSM-IV diagnosed major depression, comparing a more standardised form of practice, and use a formulated decision tree of specific evidence based intervention combinations for specific presentations. This is important to provide some internal validity for replication of results as it is possible then to say that each component used had X level of evidence and the combination of these evidence based components had X effect.

The study would need to be controlled with the naturopathic practice arm being compared with either “treatment as usual”, a validated intervention such as cognitive behavioural therapy or antidepressant therapy, or versus a novel inactive psychological technique such as ‘befriending’ via which the practitioner discusses general aspects of the person’s life without providing specific education or intervention. Furthermore where warranted a placebo tablet can be prescribed in the control group to enhance the robust experience of being treated.

Such rigorous studies would need to have the outcomes assessed via a ‘blinded’ researcher who would not know what treatment group the participant is in. Assessment of depression would need to be via validated psychiatric scales such as The Montgomery-Asberg Depression Rating Scale (Montgomery 1979) as well as self report scales such as The Beck Depression Inventory-II (Beck 1996). Additional use of cutting edge outcomes would involve analysis of participants’ genes to assess polymorphisms of key neurochemicals (such as differences of serotonin transporters) (Sarris 2011) and the analysis of serum levels of Brain-Derived Neurotropic Factor (BDNF) and cortisol, which are critical neurochemicals involved with neurogenesis (important factor in depression) (Levinson 2006).

Finally the study would need to use standardised herbal and nutritional medicines prepared via pharmaceutical good manufacturing practice.

In summary the use of a whole system research design to evaluate the efficacy and safety of naturopathic medicine as it is actually practiced will provide benefit to the profession and the public by potentially validating its therapeutic benefits. Naturalistic pilot studies such as the one detailed above provide a platform for future larger scale research using a rigorous controlled design.

Further information about the study can be found via a brief webinar video at http://www.inimh.org/inimh_videos/Libraries/INIMH_VIDEO/Naturopathy_Depression_Angerety_Study_Webinar.aspx, or on http://vimeo.com/25856980 or by emailing the author.

Acknowledgements

Dr Jerome Sarris is funded by an Australian National Health & Medical Research Council fellowship (NHMRC funding ID 628875) in a strategic partnership with The University of Melbourne and the National Institute of Complementary Medicine at Swinburne University of Technology. Thanks are extended to The NHAA, Endeavour College of Health and Integria Healthcare for supporting the study, in addition to Ms Stephanie Gadsden for assistance with the webinar and promotion.

References


continued on page 145
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- Learn what triggers microglia within the brain to initiate neurodegeneration in children
- Identify how exorphins and food additives directly affect behaviour and neurodevelopment
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- Recognise the role that allergies have in neurodevelopmental disorders
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References:
Introduction

Memory is an integral part of our existence, yet it is only vaguely understood. It is the ability to retain and utilise acquired information or knowledge. Throughout the modern history of neuroscience, memory and attention have enjoyed center stage as a fundamental process of intellectual function. Both operate together, memory has a limited capacity and hence attention determines what will be encoded. Attention operates in a world that is relatively stable over time and hence both memory and attention might reflect the same process. Attention helps to improve memory and encoding, but the details of this modulation remain unsolved (Chun 2007, Roediger 1990).

One of the most important conceptual developments in cognitive therapy is the subdivision of memory into three separate processes, encoding, storage and retrieval. Storage is difficult to study where the retrieval process is easiest to observe. A major question in many people’s minds is how to improve memory. Medications such as modafanil, donepezil and racemic amphetamine have been used to improve memory in humans. But most of them have serious adverse effects.

Recently interest in the use of herbal products has grown dramatically both in developing countries and the Western world (Sparreboom 2004). It is now apparent those available psychotherapeutic agents are not sufficient to meet the therapeutic requirements of patients with mental illness. In the folklore of Indian medicine, several herbs have been traditionally used as nerve tonics. One of the most popular of these herbs is Bacopa monnieri (BM), a well known memory booster (Husain 2007). BM, also referred to as water hyssop, brahmi or jalaminda in India, has been used for centuries in the Ayurvedic system of medicine, a holistic system of medicine originally from India. The name brahmi is derived from the word ‘brahma’ the mythical ‘creator’ in the Hindu pantheon. It is classified as a medha rasayana, a drug used to improve memory and intellect (medhya) (Mukheijee 1966). The plant has been used extensively as a nootropic and digestive and to improve learning and memory (Nadkarni 1988).

Compounds responsible for the pharmacological effect of BM include alkaloids, saponins and sterols (Bose 1931). Alkaloids such as brahmine, nicotine and herpestine have been also reported to help in its pharmacology (Chopra 1956). A major chemical entity shown to be responsible for neuropharmacological effects is bacoside (Chatterji 1965). Bacoside is a complex of bacoside A and bacoside B, probably optical isomers. It is suggested that bacoside induces membrane dephosphorylation, with a concomitant increase in protein and RNA turnover in specific brain areas (Singh 1988) and helps in motor learning (Aithal 1961). Bacoside rich extracts of BM have been evaluated for reversing depletion of acetylcholine in the frontal cortex and hippocampus (Sairam 2001).

Recently Bacopa caplets have been introduced into clinical practice. They contain extracts of Bacopa monnieri 100 mg and powders of Bacopa monnieri 650 mg to be taken in a dose of 1 caplet daily. The present study evaluated the clinical efficacy and safety of Bacopa
caplets in individuals with disturbances in concentration, memory and learning ability.

**Subjects**

Ninety six subjects who were not taking any medication or other herbal preparation and who reported no head injury, entered into the study. Before entry each subject was given a detailed description of the investigational product, nature and duration of the study. Twelve participants, seven from the placebo group and five from the drug treated group withdrew from the study after the initial testing session for personal reasons. None of them withdrew because of any adverse effect due to medication. Eighty four participants (52 females and 32 males) between the age of 30 and 42 (mean 36, SD 4) completed the study.

**Design**

The study was designed as a double blind randomised placebo control with two groups, a *Bacopa monnieri* group (n=41) and a placebo group (n=43).

**Methods**

The trial had a 3 week placebo run in with 12 weeks of treatment with either *Bacopa* or placebo. Participants were taken into the study as volunteers, living with family, taking no medication, with no complaint of memory problems and without any illness. They were educated with adequate Bengal language skills and adequately corrected vision. They were asked to refrain from alcohol for 24 hours prior to each visit and not to change life style habits during the study period. They provided informed consent and the study was approved by the local ethics committee. They were free to withdraw from the study if they so desired.

**Intervention**

The intervention was in the form of 12 weeks of a daily tablet comprising extract of *Bacopa monnieri* whole plant 100 mg and powders of *Bacopa monnieri* whole plant 650 mg. This extract was manufactured from the dried aerial plant of BM in India. The herb was extracted with water to produce 15% dry extract with a minimum of 60% of total bacoside, the plant was identified by a well qualified botanist and a voucher copy of the plant is preserved in pharmacognosy laboratory. Placebo was manufactured using excipient and replicated the active in appearance, odour and texture. Randomisation was determined by a computer generated series. All study personnel were blinded to the assignment until analysis.

**Composition**

Each caplet contains:
- Extract *Bacopa monnieri* whole plant 100 mg
- Powder *Bacopa monnieri* whole plant 650 mg

Good agricultural and collection practice (GACP) was followed during the collection and manufacture of the herbal formulation (WHO 2003). Botanical identification and Ayurvedic criteria for desired quality were in accordance with the guidelines of *Pharmacopoeial Standards of Ayurvedic Formulations* (1987) and were carried out by a qualified chemist approved by the Food and Drug Administration.

*Bacopa monnieri*, a semi aquatic herb, grows throughout India and is transplanted during September to November. Geographical source and harvest time for the herb was recorded. This formulation has been approved by regulatory authorities in India as a herbal formulation.

**Assessment**

Assessment was carried out initially and at monthly intervals until the end of the study. The assessment included a verbal memory battery designed for this study. All tasks proposed a reading input activity.

1. **Verbal span test** (Maria 2005) used to assess the general capacity of encoding verbal information. Participants read three different series of frequent words, which they were asked to recall randomly. The examiner recorded the number of words correctly recalled. The series was composed of phonologically similar words [bangle (bala), garland (mala), brother-in-law (sala)]. It also included long words such as current or running (cholito bhasha), name (pundarikaksha), guest (aaguntak), sweet (jolbharad sondesh), poem (shesher kovita).

2. **Verbal working memory task** (Daneman 1980) consists of reading several long sentences while retaining in memory the last word of each sentence. Participants were presented with three series of sentences and asked to recall the last word of each sentence.

3. **Text comprehension test** (logical memory) (Kintsch 1978). A story was presented to the participants and the subject was asked to recall the information in the text with details after reading it once.

   - For each compiled task the subject received 1 point or a 0 score; in the repetitive tasks the maximum score was 2; the event based task was 4.

**Safety test**

The subjects underwent hematological evaluation on entry and at the end of the study. All adverse events either reported or observed by patients were recorded with information about severity, duration and action taken regarding the study drug. The relationship of adverse events to the study medication was prede ned as ‘unrelated’ (a reaction that does not follow a reasonable temporal sequence from the time of administration of the drug), ‘possible’ (follows a known response pattern to the suspected drug but could have been produced by the patient’s clinical state or other modes of therapy administered to the patient), and ‘probable’ (follows a known response pattern to the suspected drug that could not be reasonably explained by the known characteristics of the patient’s clinical state). For patients recorded
as withdrawing from the study, efforts were made to ascertain the reason for the dropout. Non compliance (defined as failure to take less than 80% of the medication) was not regarded as treatment failure and reasons for non compliance were recorded.

**Primary and secondary outcome measures**

The predefined primary outcome measure was the effect of BM on memory and learning ability. The predefined secondary outcome was incidence of adverse effects and patient compliance.

**Statistical analysis**

Statistical analysis was carried out using Fisher’s Exact test for presence or absence of various signs. Repeated measures of ANOVA followed by Dunnett’s Multiple comparison and Posthoc were used for analysis of hematological parameters. Changes in memory and learning ability were analysed using paired ‘t’ test. Values were expressed mean ± SD. The minimal level of significance was fixed at p<0.05. Statistical analysis was carried out using GraphPad Prism version 4.03.

**Results**

There were 96 subjects who were available for recruitment, 12 withdrew for personal reasons. The majority of the subjects were women of Asian origin. Average age was 36.0±4 and educational level was high school (Table 1). No difference existed between the groups for age, blood pressure, heart rate, temperature or education level. Mean score for tests of memory and learning are shown in Table 2. Bacopa drug therapy significantly improved verbal span memory, verbal working memory and logical memory at 16 weeks of drug therapy; placebo group did not show any such change. Placebo run in period did not indicate any significant changes in any of the parameters. Similarly no significant effects were observed on blood pressure, hematology, liver function tests, renal function test and fasting blood sugar.

<table>
<thead>
<tr>
<th>Table 1: Demographic data</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (mean ± SD) years</td>
</tr>
<tr>
<td>36.0±4</td>
</tr>
<tr>
<td>Sex M/F</td>
</tr>
<tr>
<td>Education status</td>
</tr>
<tr>
<td>Mean blood pressure</td>
</tr>
</tbody>
</table>

**Discussion**

The present study indicates that Bacopa caplets when given for sixteen weeks are well tolerated in adults and help in improvement in cognitive function. Bacopa improved verbal span tests, verbal working memory task and text comprehension task where placebo recipients remained stable on these tasks. The benefits of Bacopa in cognitive functions have been reported in a number of other studies (Stough 2001, Roodenrys 2002).

The exact mechanism of action of Bacopa in enhancing mental activity is unknown, however the

<table>
<thead>
<tr>
<th>Table 2: Mean score for memory and learning tests</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bacopa (n = 41)</td>
</tr>
<tr>
<td>Task</td>
</tr>
<tr>
<td>Verbal span:</td>
</tr>
<tr>
<td>Short words</td>
</tr>
<tr>
<td>Long words</td>
</tr>
<tr>
<td>Verbal working memory</td>
</tr>
<tr>
<td>Logical memory</td>
</tr>
</tbody>
</table>

**Table 3: Effect of drug therapy on hematological parameters**

<table>
<thead>
<tr>
<th>Parameters</th>
<th>Before treatment</th>
<th>After treatment</th>
<th>Before treatment</th>
<th>After treatment</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bacopa monnieri</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Haemoglobin (gm/dl)</td>
<td>13.23±1.15</td>
<td>13.55±2.14</td>
<td>13.00±1.31</td>
<td>14.50±1.52</td>
</tr>
<tr>
<td>E.S.R. (mm/hr)</td>
<td>6.16±1.74</td>
<td>5.10±1.55</td>
<td>8.33±2.05</td>
<td>7.55±1.05</td>
</tr>
<tr>
<td>Total WBC count (cells/cu.mm3)</td>
<td>6453.00</td>
<td>6250.00</td>
<td>6671.00</td>
<td>6570.50</td>
</tr>
<tr>
<td>SGPT</td>
<td>IU/L</td>
<td>17.42</td>
<td>16.45</td>
<td>18.21</td>
</tr>
<tr>
<td>SGOT</td>
<td>IU/L</td>
<td>22.22</td>
<td>23.50</td>
<td>24.55</td>
</tr>
<tr>
<td>Serum creatinine</td>
<td>mg/dL</td>
<td>0.96</td>
<td>0.98</td>
<td>0.94</td>
</tr>
<tr>
<td>Total bilirubin</td>
<td>mg/dL</td>
<td>1.0</td>
<td>0.5</td>
<td>0.8</td>
</tr>
<tr>
<td>Mean FBS (mg %)</td>
<td>94.40</td>
<td>90.50</td>
<td>94.00</td>
<td>90.50</td>
</tr>
<tr>
<td>SD 8.53</td>
<td>9.57</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
triterpenide saponins and their bacosides are responsible for the ability of *Bacopa* to enhance nerve impulse transmission. The bacosides aid in repair of damaged neurons by enhancing kinase activity, neuronal synthesis and restoration of synaptic activity (Singh 1997). Studies have also indicated that *Bacopa* extract modulates the expression of certain enzymes involved in generation and scavenging of reactive oxygen species in the brain (Chowdhuri 2002). Therapeutic doses of *Bacopa* are not associated with any known side effects and *Bacopa* has been used safely in Ayurvedic medicines for several hundred years.

Further studies may be required to determine whether the advantageous effects of *Bacopa* are due to its direct effect on brain chemistry to influence memory processes. A larger sample size will be useful for pharmacovigilance.

**Conclusion**

The present study indicates that *Bacopa* caplets are safe and efficacious in improving cognitive functions in human subjects. *Bacopa* drug therapy significantly improved verbal span memory, verbal working memory and logical memory at 16 weeks of drug therapy. The formulation is safe without any serious adverse effects. The drug is well tolerated.

**References**


**Disclosure of conflicting interest**

Dr Pralhad S Patki and Dr Suprabha Hegde are full time employees of The Himalaya Drug Company. Dr Asim Kumar Mandal is a clinical tutor at Kolkata and has no financial interest in The Himalaya Drug Company.
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**Turmeric Curcuminoids 500**

Potent Anti-Inflammatory & Antioxidant
Each capsule contains:
Curcumin 526mg equiv. to 500mg Curcuminoids of Curcuma longa (C3 Curcumin Complex®)

**Dosage Adults:**
Take 1-2 capsules, once or twice a day with water, or as professionally prescribed.

**Presentation:**
60 Capsules  Product Code: 17133  AUST L: 163424

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**Fenugreek**

Promotes Healthy Lactation & Respiratory Expectorant
Each capsule contains:
Trigonella foenum-graecum (Fenugreek) seed powder 529mg

**Dosage Adults:**
Take one to two capsules with a meal three times daily.

**Presentation:**
100 Capsules  Product Code: 17078  AUST L: 26008

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**Hawthorn Berries**

Traditional Circulatory System Function Support
Each capsule contains:
Crataegus laevigata (Hawthorn berries) fruit powder 450mg

**Dosage Adults:**
Take two capsules with a meal twice daily or as directed by your healthcare practitioner.

**Presentation:**
100 Capsules  Product Code: 17017  AUST L: 25448

---

**Pau D’Arco**

South American Anti-Fungal Herb
Each capsule contains:
Tabebuia heptaphylla (Pau D’Arco) inner stem bark powder 500mg

**Dosage Adults:**
Adults : Take two capsules three times daily with a meal.
Children 6-12 years : Take one capsule twice daily with a meal.

**Presentation:**
100 Capsules / 270 Capsules  Product Code: 17002 / 17126  AUST L: 25926

---

**Slippery Elm**

Helps Soothe an Unsettled Stomach
Each capsule contains:
Ulmus rubra (Slippery elm) bark powder 360mg

**Dosage Adults:**
Adults : Take two capsules twice daily before or after a meal.
It is recommended to drink plenty of water throughout the day.

**Presentation:**
100 Capsules / 270 Capsules Product Code: 17000 / 17124  AUST L: 181873
Anticancer activity of *Mayodendron igneum*, Kurz family Bignoniaceae

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Introduction

*Mayodendron igneum* Kurz Fam. Bignoniaceae, also known as *Radermachera ignea* Kurz, grows wildly in north Myanmar, north Thailand, Laos, Vietnam and south China. It is also planted as a vegetable, for medicinal uses and in home gardens of south Yonnan, as an ornamental (Chun-lin 1990).

The biological screening of fractions derived from leaves of some plants of Bignoniaceae such as *Macfadyena unguis-cati* have revealed antitumoral, antitrypanosomal and anti-inflammatory activities (Duarte 2000). Ogura et al (1977b) isolated from *Jacaranda caucana* Pittier a phytoquinoid derivative *jacaranone* which exhibited both in vitro cytotoxic and in vivo antitumor activity against the P-388 lymphatic leukemia system. Itokawa et al (1992) proved that the alcoholic extract of *Mansoa alliacea* shows cytotoxic activity against V-29 cells, due to the presence of lapachol, which exhibits potent antitumor activity. Bioactive naphthoquinones isolated from *Tabebuia barbata* by Colman-de Saizarbitoria et al (1977) were found to be active against A-549 human lung adenocarcinoma, MCF-7 breast carcinoma and HT-29 human colon carcinoma.

Alguacil et al (2000) examined aqueous and alcoholic extracts of pods and flowers of *Tecoma sambucifolia* in vitro toxicity in Chinese hamster ovary cells, human hepatoma cells and human larynx epidermal carcinoma cells. The highest cytotoxicity was noted with the alcoholic extracts where the human hepatoma cell line was the most sensitive, especially to the alcoholic extract of flowers. The triterpenoid ursolic acid isolated from the petroleum ether extract of *Jacranda caucana* and *Tecoma radicans* has in vitro cytotoxic activity (Ogura 1977, Hashem 2006).

Diet is the single greatest contributor to human cancer and may be associated with a 35%-70% incidence of the disease. Although various carcinogens are present in foods, their effects are minor compared with dietary components that inhibit the cancer process. The crude extract (80% alcohol) of leaves of *Mayodendron igneum* Kurz, Bignoniaceae was examined for its cytotoxic activity against different cell lines. It showed higher activity against liver, cervix and breast cell lines, IC₅₀ (0.87, 0.60 and 0.54 µg from antitumor activity. Bioactive naphthoquinones isolated due to the presence of lapachol, which exhibits potent

Experimental

Plant material

The fresh nonflowering aerial part of *Mayodendron igneum* Kurz, Bignoniaceae, was collected from Giza Zoo of Egypt in June 2008. A voucher specimen of the plant (voucher number M20) was identified by Mrs. Treeze Labib, Specialist in Plant Taxonomy, Orman Garden (Botanical garden of Egypt.)

Total ethanol extract

Total ethanol extract (crude extract) was prepared by percolating 500 g dry powder with 80% ethanol to exhaustion, the filtered percolate was concentrated under vacuum at 40°C. The yield was 28.75% w/w.

Preparation of successive extracts

Powder air dried nonflowering aerial parts of *Mayodendron igneum* (500 g) were successively extracted in a Soxhlet apparatus using petroleum ether, chloroform, ethyl acetate and ethanol 95%. These extracts were evaporated to dryness under vacuum at 40°C yielding dark oily residues (8.4, 17.68, 1.55 and 13.8% w/w of solvent free extracts).

Isolation of flavonoids

The ethyl acetate fraction was examined by paper chromatography (Whatmann No 1) using the solvent systems n-butanol; acetic acid; water (3:1:1) (a) and 15% acetic acid (b). Chromatograms were visualised under UV, UV & NH₃, and UV & AlCl₃. The presence of the detected spots in the extract, their Rₐ values and colours were recorded. These compounds were isolated by preparative paper chromatography on Whatmann 3MM using solvent system (a), then purified by repeated PPC using solvent system (b). The final purification was performed on Sephadex LH-20 column and elution was with methanol.
Characterisation of compounds

Table 1: Chromatographic properties of isolated flavonoids

<table>
<thead>
<tr>
<th>Compound number</th>
<th>Solvent system a</th>
<th>Solvent system b</th>
<th>UV</th>
<th>UV/NH₃</th>
<th>AlCl₃/UV</th>
</tr>
</thead>
<tbody>
<tr>
<td>I</td>
<td>0.18</td>
<td>0.15</td>
<td>purple</td>
<td>yellow green</td>
<td>yellow</td>
</tr>
<tr>
<td>II</td>
<td>0.39</td>
<td>0.13</td>
<td>purple</td>
<td>yellow</td>
<td>yellow</td>
</tr>
<tr>
<td>III</td>
<td>0.47</td>
<td>0.27</td>
<td>purple</td>
<td>yellow</td>
<td>yellow</td>
</tr>
<tr>
<td>IV</td>
<td>0.80</td>
<td>0.13</td>
<td>purple</td>
<td>yellow green</td>
<td>yellow</td>
</tr>
<tr>
<td>V</td>
<td>0.75</td>
<td>0.08</td>
<td>purple</td>
<td>yellow</td>
<td>yellow</td>
</tr>
</tbody>
</table>

Table 2: UV spectral data of the isolated flavonoids

<table>
<thead>
<tr>
<th>Compound number</th>
<th>Methanol</th>
<th>NaOMe</th>
<th>AlCl₃</th>
<th>AlCl₃/HCl</th>
<th>NaOAc</th>
<th>NaOAc/H₃BO₃</th>
</tr>
</thead>
<tbody>
<tr>
<td>I</td>
<td>274, 334</td>
<td>272, 301 (sh), 389</td>
<td>265, 298 (sh), 357, 389</td>
<td>274, 298 (sh), 342, 382</td>
<td>274, 355, 387</td>
<td>270, 340</td>
</tr>
<tr>
<td>II</td>
<td>255, 270 (sh), 339</td>
<td>265, 396</td>
<td>266, 298 (sh), 359, 422</td>
<td>272, 294 (sh), 356, 387</td>
<td>268, 365 (sh), 406</td>
<td>261, 366</td>
</tr>
<tr>
<td>III</td>
<td>259, 338 (sh), 360</td>
<td>272, 340 (sh), 410</td>
<td>272, 305 (sh), 338 (sh), 430</td>
<td>270, 305 (sh), 360, 405</td>
<td>270, 337 (sh), 380</td>
<td>260, 337 (sh)</td>
</tr>
<tr>
<td>IV</td>
<td>267, 336</td>
<td>275, 325, 392</td>
<td>276, 300, 348, 364</td>
<td>276, 299, 340, 381</td>
<td>275, 301, 376</td>
<td>268, 302 (sh), 338</td>
</tr>
<tr>
<td>V</td>
<td>253, 267 (sh), 291 (sh), 349</td>
<td>266 (sh), 329 (sh), 401</td>
<td>275, 300 (sh), 328, 426</td>
<td>266 (sh), 275, 355, 385</td>
<td>269, 326 (sh), 384</td>
<td>259, 301 (sh), 369, 425 (sh)</td>
</tr>
</tbody>
</table>

Table 3: ¹H-NMR of isolated flavonoids in DMSO

<table>
<thead>
<tr>
<th>Proton number</th>
<th>I 500 MHz</th>
<th>II 500 MHz</th>
<th>III 500 MHz</th>
<th>IV 500 MHz</th>
<th>V 500 MHz</th>
</tr>
</thead>
<tbody>
<tr>
<td>3</td>
<td>6.75(s)</td>
<td>6.65(s)</td>
<td>6.70(s)</td>
<td>6.70(s)</td>
<td>6.50(s)</td>
</tr>
<tr>
<td>6</td>
<td>6.40 (d,j=2Hz)</td>
<td>6.35 (d,j=2Hz)</td>
<td>5.94 (d,j=2Hz)</td>
<td>6.35 (d,j=2Hz)</td>
<td>6.25 (d,j=2Hz)</td>
</tr>
<tr>
<td>8</td>
<td>6.80 (d,j=2Hz)</td>
<td>6.75 (d,j=2Hz)</td>
<td>6.10 (d,j=2Hz)</td>
<td>6.75 (d,j=2Hz)</td>
<td>6.65 (d,j=2Hz)</td>
</tr>
<tr>
<td>2′</td>
<td>7.90</td>
<td>7.30 (d,j=2Hz)</td>
<td>7.22 (d,j=2Hz)</td>
<td>7.90 (d,j=8.5Hz)</td>
<td>7.30 (d,j=2Hz)</td>
</tr>
<tr>
<td>6′</td>
<td>7.90 (d,j=8.5Hz)</td>
<td>7.40 (d,d,j=8.5 &amp; 2Hz)</td>
<td>7.48 (d,d,j=8.5 &amp; 2Hz)</td>
<td>7.90 (d,j=8.5Hz)</td>
<td>7.40 (d,j=8.58, 2.1Hz)</td>
</tr>
<tr>
<td>3′</td>
<td>6.90 (d,j=8.5Hz)</td>
<td>7.00 (d,j=8.5Hz)</td>
<td>7.00 (d,j=8.5Hz)</td>
<td>6.90 (d,j=8.5Hz)</td>
<td>6.90 (d,j=8.5Hz)</td>
</tr>
<tr>
<td>5′</td>
<td>6.90 (d,j=8.5Hz)</td>
<td>5.05 (d,d,j=7.5Hz)</td>
<td>7-O-glucosyl</td>
<td>6.80 (d,j=8.5Hz)</td>
<td>6.90 (d,j=8.5Hz)</td>
</tr>
<tr>
<td>H-1″</td>
<td>5.00 (d,j=7.5Hz)</td>
<td>5.05 (d,d,j=7.5Hz) 7-O-glucosyl</td>
<td>5.40 (d,j=7.5Hz) 3-O-glucosyl</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Apparatus

¹H-NMR Spectrophotometer Jeol EX 270, 300 and 500 NMR spectrometer. ¹³C-NMR spectrophotometer Jeol EX, 75 and 125 spectrometer. Ultraviolet visible recording spectrophotometer, UV-VIS. Double Beam, UVD-3500, Lambomed Inc.

Investigation of cytotoxic activity of total ethanol extract of Mayodendron igneum by SRB assay

Potential cytotoxicity of 80% ethanol extract of Mayodendron igneum was tested using the method of Skehan et al (1990).

1. The total ethanol extract of the plant was tested for cytotoxic activity against the following human tumor cell lines: HEPG2 liver, HCT116 colon, HELA cervix, HEPL2 larynx, MCF breast.
2. Tumor cells were plated in 96-multiwell plate (10⁶ cells/well) for 24 h before treatment with the extract to allow attachment of cells to the wall of the plate.
3. Different concentrations of extract (0, 1, 2.5, 5 and 10 µg/mL DMSO) were added to the cell monolayer. Triplicate wells were prepared for individual doses.
4. Monolayer cells were incubated with extract for 48 h at 37°C in atmosphere of 5% CO₂.
5. After 48 h cells were fixed, washed and stained with...
sulforhodamine B stain (Sigma).
6. Excess stain was washed with acetic acid and attached stain recovered with Tris EDTA buffer (Sigma).
7. Colour intensity was measured in an ELISA reader.
   The relation between surviving fraction and extract concentration was plotted to get a survival curve of each tumor cell line after incubation with the extract.
   The potency of the extract was compared with reference Doxorubicin (Merck, Germany).
8. The same method repeated on successive extracts using the cell lines showed lowest survival fractions, liver, cervix and breast.

Results and discussion
Identification of compounds
The purified compounds were subjected to UV, 1H-NMR and 13C-NMR spectral analysis. The chromatographic properties and UV data of these compounds were compared with published data (Mabry 1970, Markham 1982).

Compound I
Compound I was isolated from ethyl acetate fraction with deep purple colour on paper chromatography at Rf (a) 0.18 and Rf (b) 0.15 under UV, changed to yellow green on NH3 exposure. Upon acid hydrolysis compound I gave apigenin in the lipophilic layer and glucose in the hydrophilic layer. From UV data it was observed that compound I has free hydroxyl group at C-5 and free OH at C-4’. The difference in band I in methanol (330 nm) after addition of sodium methoxide (389 nm) was ac 59 nm with increase in intensity. No shift in band II after addition of NaOAc attributed to 7-O-glucosylation.

No ortho dihydroxyl groups were observed after addition of AlCl3/HCl compared with AlCl3. The 1H NMR spectrum revealed the characteristic signal of apigenin nucleus: a pair of A2B2 aromatic system protons at δ ppm: 7.90 (d, J=8.5 Hz, 2H) and 6.90 (d, J=8.5 Hz, 2H) for H-2’, 6’ and H-3’, 5’ respectively. Two meta coupling signals at δ ppm: 6.40 (d, J=2 Hz, 1H) for H-6 and at 6.80 (d, J=2 Hz, 1H) for H-8 and a singlet centered at 6.75 for H-3. This downfield shift of both H-6 at δ ppm: 6.40 and H-8 at 6.80 relative to the corresponding positions in apigenin ( Markham 1982) indicated the attachment of the glucose residue to C-7 of the aglycone.

The 1H NMR spectrum also revealed the anomeric proton of glucose moiety at δ ppm: 5.00 (d, J= 7.5 Hz, 1H) showing the β-configuration of glucose. Compound I was found to be apigenin-7-O-β-glucopyranoside.

Compound II
Compound II was isolated from ethyl acetate fraction with deep purple colour on paper chromatography at Rf (a) 0.39 and Rf (b) 0.13 under UV, changed to yellow green on NH3 exposure. Upon acid hydrolysis compound II gave luteolin in the lipophilic layer and glucose in the hydrophilic layer. From UV data it showed luteolin skeleton: UV spectrum in methanol gave characteristic band I at λmax 340 nm and band II at 255 nm of a luteolin nucleus (Mabry 1970). The difference in band I in MeOH (340 nm) and after NaOMe addition (396 nm) was ca 56 nm indicated free hydroxyl group at position 5, the increase in intensity in band I indicated free OH at 4’ position. No bathochromic shift in band II after addition of NaOAc indicated the glucosylation of 7-OH.

The difference in band I in AlCl3/ HCl (387 nm) compared with AlCl3 (422) was ca 35 nm indicated the presence of ortho dihydroxyl groups at 3’ and 4’ positions. 1H NMR spectrum showed an ABX coupling system at δ ppm: 7.40 (dd), 7.30 (d) and 7.00 (d) assigned to H-6’, H-2’ and H-5’ respectively for 3’, 4’ dihydroxy B-ring. Two meta doublets at δ ppm: 6.75 and 6.35 assigned to H-8 and H-6 respectively. The δ and J values of the anomeric proton signal (5.00 ppm and 7.5 Hz) were diagnostic evidences for β-configuration of the glucose moiety at C-7 position. Compound II was identified as luteolin-7-O-β-glucopyranoside.

Compound III
Compound III showed deep purple colour on paper chromatography at Rf (a) 0.47 and Rf (b) 0.27 under UV, changed to yellow on NH3 exposure. Upon acid hydrolysis compound III gave quercetin in the organic phase and glucose in the aqueous phase. The UV data revealed that the glucosylation was in position 3. This was shown by the difference of band I between the MeOH spectrum and AlCl3/ HCl was ca 45 nm.

The increase in intensity of band I with NaOMe was indicative of a free 4’-OH group. The free 7-OH was confirmed by a bathochromic shift upon addition of NaOAc compared to MeOH spectrum (ca 11 nm). The ortho dihydroxyl group in ring B was detected by a hypsochromic shift of band I after addition of AlCl3/ HCl compared to AlCl3, spectrum (ca 25 nm). 1H NMR spectrum showed a double doublet at δ ppm: 7.48, attributable to H-6’, a doublet at 7.22 attributable to H-2’ and a doublet at 6.80 attributable to H-5’. Two meta doublet at δ ppm: 6.10 and 5.94 assigned to H-8 and H-6 respectively. 1H NMR spectrum showed the anomeric proton of glucose at δ ppm: 5.40 (d, J=7.5 Hz, 1H), indicative to the attachment of glucose residue to C-3 of the aglycone. Thus compound III was identified as Quercetin-3-O-β-glucopyranoside.

Compound IV
Compound IV showed a deep purple colour on paper chromatography at Rf (a) 0.80 and Rf (b) 0.13 under UV, changed to yellow green on NH3 exposure. The chromatographic properties of compound IV showed that it was an aglycone. The UV data was as compound I except upon addition of NaOAc, compound IV had a bathochromic shift (275 nm) compared with MeOH spectrum (267 nm) indicative to the presence of free 7-OH. Compound IV was identified as apigenin.
Compound V

Compound V showed a deep purple color on paper chromatography at Rf (a) 0.75 and Rf (b) 0.08 under UV, changed to yellow on NH3 exposure. The chromatographic properties of compound V showed that it was an aglycone. The UV data was as compound II except upon addition of NaOAc, compound V had a bathochromic shift (269 nm) compared with MeOH spectrum (253 nm) indicative to the presence of free 7-OH. Compound V was identified as luteolin.

Cytotoxic activity of Mayodendron igneum extracts by SRB assay

Extracts of many plants of the Bignoniaceae family were tested for their cytotoxicity or antitumor activity. The crude extract (80% alcohol) of leaves of Mayodendron igneum was examined for antitumor activity against different cell lines by the method of Skehan et al (1990). The results obtained were compared with that produced from Doxorubicin Merck, Germany, as a reference drug. (See www.nhaa.org.au under Publications, AJMH, downloads for figures on the cytotoxic activity of total ethanol extract and successive extracts of M. igneum Kurz compared with Doxorubicin on different cell lines.)

Table 4 comprising the effect of the ethanol extract of Mayodendron igneum Kurz on different cell lines, shows a high inhibition effect on the survival fraction and very high activity against liver, cervix and breast cell lines (IC50, 0.87, 0.60 and 0.54 μg respectively).

When the successive fractions isolated from the leaves of Mayodendron were tested against these three cell lines, petroleum ether, chloroform and ethyl acetate extracts showed high activity against liver and breast cell lines, while ethanol extract was a more potent inhibitor of breast carcinoma.

Table 4: IC50 results of the total ethanol extract and the successive extracts of M. igneum Kurz compared with doxorubicin on different tumor cell lines

<table>
<thead>
<tr>
<th>Tumor cell line type</th>
<th>IC50 of total ethanol extract (µg/mL)</th>
<th>IC50 of petroleum ether extract (µg/mL)</th>
<th>IC50 of chloroform extract (µg/mL)</th>
<th>IC50 of ethyl acetate extract (µg/mL)</th>
<th>IC50 of ethanol extract (µg/mL)</th>
<th>IC50 of doxorubicin extract (µg/mL)</th>
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References

Medicinal plants used for dermatological disorders: a study of Uttarakhand State in India

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Introduction

Since the human skin is directly exposed to the outer environment, it is the most sensitive body part to changes in the environment and hence most susceptible to diseases based on environmental health. Being a barrier and defensive layer between pathogens including external damages and internal environment of human body the skin not only functions as the protection but also contains a variety of nerve endings that react to heat, cold, pressure, vibration and tissue injury (Madison, 2003, Proksch 2008). The skin regulates heat, acts as a storage center for lipids and water and is a water resistant barrier preventing loss of essential nutrients from the body (Connor 2003, Madison 2003, Proksch 2008). Therefore any abnormality in skin and its function may have a large impact on human health due to increasing susceptibility of internal body organs to the external environment.

Historically skin diseases have had serious impacts on the quality of human life across the world. Some 3000 varieties of skin diseases, including many rare ones, are known to medical science (Anon 2005). Despite this fact skin diseases generally have been given low priority by health authorities. Although many people do not see these diseases as a major problem, skin diseases impose a severe impact on wellbeing. Many skin diseases have a long history and in many cases are restricted to geographical areas and the local culture. Besides a number of environmental factors, heredity plays an important role in transmission of some skin diseases from one generation to another (Thappa 2009). Skin cancer is the most common form of cancer in some developed countries, even though it is largely preventable.

Although little attention is being paid to skin diseases in comparison to other fatal diseases, skin diseases are among the most common diseases seen in the primary health care setting in tropical areas, causing unnecessary suffering and even death. At any given time one out of every three people in the United States suffers from a skin disease (Thorpe 2004, Anon 2005). The World Health Organisation showed that skin diseases were associated with mortality rates of 20 000 in Sub Saharan Africa in 2001 (Mathers 2006). Although mortality rates are comparatively lower than other diseases, skin diseases are common and enhance morbidity through disfigurement, disability or symptoms such as intractable itch, reducing the quality of life (Hay 1994). In America skin diseases are placed in the top 15 groups of medical conditions for which the health care costs have grown since 1987 (Thorpe 2004).

In the present era of global climate change with the explosion of human population and increasing interactions among people of different countries, the risk of spreading skin related diseases is quite high. Learning the causes and practices used in curing skin diseases can help people to make better choices and reduce the risk of developing disabling and potential deadly diseases. This study was conducted in the Uttarakhand state of India with a view to understanding the use of plant species for curing various skin diseases.

Methods

Study area

The Indian state of Uttarakhand is well known for its rich biodiversity and cultural mosaic of diverse nature.
The state is comprised of 13 districts and is bounded on the northwest by Himachal Pradesh, on the north by Tibet (China), on the east by Nepal, and on the south by Uttar Pradesh. The state possesses a wide altitudinal range from 210 m to 7,817 m over the total area of 53,485 km². Uttarakhand covers about 12.18% of the total Indian Himalaya, 40% of its total area falls under different forest types, some of the major vegetation types classified along the altitudinal gradient are tropical, sub tropical, temperate, sub alpine and alpine (Kala 2010).

The total human population of the state is close to 8,480,000 of which 78% live in rural areas. Due to the geographical diversity and inaccessibility, a well known feature of the mountainous region, Uttarakhand has remained isolated from the rest of the agricultural plains of northern India and has thus preserved some of the old practices, traditions and ethnic norms for various resource use patterns. The sociocultural fabric in this region is characterised by diverse ethnic groups which have developed their own cultures based on available natural resources, giving rise to a cultural diversity. The rich plant diversity, geographical isolation and long period of people dependency on plants for curing diseases are some of the important factors for selection of Uttarakhand to carry out the present study.

**Survey methods**

**Secondary sources**


**Fieldwork**

Although the majority of information was collected from secondary sources, field surveys were also undertaken for gathering data on the availability and uses of medicinal plant species across various localities in the study area from tropical to alpine zones. The survey focused on collecting information using a semistructured questionnaire on types of ailments being cured by the traditional use of medicinal plants and plant parts used.

The information on skin diseases and their treatments was gathered from 60 traditional herbal healers. The healers were selected randomly for interviewing from a list of 200 traditional healers who were identified during community workshops. Five workshops were organised in different districts of Uttarakhand and various groups of indigenous people including herbal healers were invited to interact and help in documentation of their knowledge on medicinal plants for curing diseases. The data was cross checked by interviewing more than three healers on the specific uses of a plant species. In order to verify the identity of medicinal plant species field visits were undertaken with herbal healers.

**Results**

A large number of medicinal plants growing in various habitats and elevations were used by local people of Uttarakhand for curing dermatological problems. The present study resulted in the documentation of 132 plant species of which herbaceous plants were highest (n=77) followed by trees (26), shrubs (25) and 2 each in under shrub and woody climbers (Table 1). Species were used for curing 19 different types of skin diseases including frost bite, goiter, pimples, itching, eczema, leprosy, sores, bruises, carbuncles, burns, small pox, scabies, boils, gout, removal of lice, blisters, swelling, septic wounds, cuts and wounds (Table 2). Most of the species were used for curing a limited number of skin diseases, whereas a few species were used for curing over 5 types of skin diseases. Agerotum cornyzoideus was used in curing 9 types of skin diseases including burns, septic wounds, scabies, swelling, boils, sores and cuts and wounds. Azadirachta indica, Vext negundo, Woodfordia fruticosus, Allium cepa, Cuscuta reflexa, Shorea robusta and Skimmia laureola were other important species in their uses for curing 4-5 types of skin related diseases.

There were variations in the species used for curing particular skin diseases by the local people and traditional herbal healers. A total of 65 plant species were used for curing cuts and wounds, the highest number of species used for curing one particular type of skin related problem. Contrary to this Solanum nigrum was the only species used by healers and documented during the present investigation for treatment of goiter. Similarly for treatment of frost bite Juglans regia and Solanum tuberosum were the only herbs used. A total of 22 plant species were used in treatment of sores, 21 for boils, 17 for swelling, 15 each for leprosy and scabies, 13 for septic wounds, 12 for eczema, 11 for burns, 8 for small pox and 7 for itching.

The plant species used for skin diseases is dependent on their availability in nature. Of 132 medicinal plant species the following 22 are considered rare and endangered; Aconitum atrox, Dactylorhiza hatagirea, Fritillaria roylei, Thalictrum foliolosum, Berberis aristata, Artemisia maritime, Delphinium cashmerianum, Gloriosa superb, Saussurea obvallata, Betula utilis, Nardostachys jatamansi, Swertia chiraita, Rheum austral, Rheum webbianum, Podophyllum hexandrum, Hippophea salicifolia, Bergenia ligulata, Bergenia stracheyi, Arnebia penthamii, Rhododendron arboratum, Aegle marmelos, Lyonia ovalifolia and Waldhermia glabra.

Although the specific uses of species for skin ailments were disclosed by the interviewees, the specific dermatological use of 14 plant species was not disclosed, only that the species was used for certain types of skin diseases. These species were Arisaema jacquemontii, Artemisia japonica, Astragalus candidleanus, Berberis...
jaeschkeana, Chenopodium album, Convolvulus arvensis, Corydalis govaniana, Jasminum humile, Raphanus sativus, Saussurea costus, Thymus linearis, Arnona squamosa, Papulia lappacea and Drosera peltata.

**Discussion**

Traditionally the knowledge of treating skin diseases in India was restricted to a few specialised herbal healers and generally passed from one generation to another by word of mouth. Written documents were limited in which only a few dermatological problems were described. It is reported that the knowledge of allergic diseases harmful to the skin did not exist at that time (Thappa 2009). In 1991 the Ministry of Health and Family Welfare, Government of India had about 2000 dermatologists for a population of 843 million. Although the situation has now changed and the number of dermatologists has increased, these dermatologists are concentrated in the cities and large towns (Thappa 2002). It is estimated that one in 20 people in India has some kind of skin disease (Kumar 1996). Seventy five percent of India’s population lives in rural areas, with such a large population mainly treated by traditional healers with the help of bioresources available in the village and surrounding forest areas.

Furthermore the modern system of medicine is unable to afford treatments for all types of skin diseases. There are reports claiming shortage of basic skills in the management of skin diseases hence the failure rate of treatment is quite high (Figueroa 1998, Hiletework 1998). However the treatment of skin diseases using medicinal plants in Uttarakhand is quite common and effective. The local people of adjacent areas of Uttarakhand such as Himachal Pradesh, use 18 species of medicinal plants for treating 6 types of skin disease, of these the highest number was used for the treatment of boils, followed by healing of cuts and wounds (Lal 2008).

The environmental degradation and pollutants are also responsible for causing skin diseases. Many people have developed sensitivities to different pollen grains causing skin allergies. The local people of Uttarakhand perceive that the pollen grains of chir pine are the source of a skin allergy (Kala 2010). Skin diseases are often infectious and transmissible. The intensity of disease may vary with the environmental and climatic conditions. Fungal infections commonly affect skin during the rainy season. Such infection causes irritation and discomfort. The use of Azadiracta indica for removing such fungus from the skin is considered quite effective.

Although the healers did disclose the specific uses of most of the plant species used, it was noticed that for some specific treatments healers would not disclose their procedures. This may be one of the ways of a traditional patent system, which not only helps the healers in protecting their intellectual knowledge but also protect the species from overexploitation.

Many medicinal plant species have become rare and endangered partly due to overharvesting from nature in the recent past. There is now a ban on collection of many such plant species from the wild, however many of these species are essential for making particular types of herbal formulations for skin diseases. The herbal healers admit that they face difficulty in making those specific formulations due to less availability and bans on collection of some rare and endangered species (Kala 2000, 2005). The low availability of such plant species has affected the traditional system of plant use for treating specific skin diseases.

Since the modern system of medicine is unable to afford treatments for all types of skin diseases, the effective treatment of skin diseases by using medicinal plants, as evident from the Uttarakhand state of India, will help to improve the quality of human life. Therefore attempts need to be made to strengthen the alternative system of medicine in view of its wide acceptability, effectiveness and centuries of practical experimentation, especially in developing countries.

**References**


### Table 1: Medicinal plants and plants parts used for treatment of dermatological problems

<table>
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<th>No</th>
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<th>Habit</th>
<th>Plant part used</th>
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</thead>
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<td>Lambertia camera</td>
<td>Shrub</td>
<td>Fruit, Leaf</td>
</tr>
<tr>
<td>74</td>
<td>Leonia ovalifolia</td>
<td>Tree</td>
<td>Stem, Leaf, WP</td>
</tr>
<tr>
<td>75</td>
<td>Malvastrum emondulatum</td>
<td>U Shrub</td>
<td>Leaf</td>
</tr>
<tr>
<td>76</td>
<td>Melia azederach</td>
<td>Tree</td>
<td>Fruit, Leaf</td>
</tr>
<tr>
<td>77</td>
<td>Mentha longifolia</td>
<td>Herb</td>
<td>Whole plant</td>
</tr>
<tr>
<td>78</td>
<td>Morus alba</td>
<td>Shrub</td>
<td>Fruit, Bark</td>
</tr>
<tr>
<td>79</td>
<td>Nardostachys jatamans</td>
<td>Herb</td>
<td>Rhizome</td>
</tr>
<tr>
<td>80</td>
<td>Neolitsea pallens</td>
<td>Tree</td>
<td>Fruit</td>
</tr>
<tr>
<td>81</td>
<td>Ocimum sanctum</td>
<td>Herb</td>
<td>Leaf, Seed, WP</td>
</tr>
<tr>
<td>82</td>
<td>Ophioglossum vulgarum</td>
<td>Herb</td>
<td>Rhizome</td>
</tr>
<tr>
<td>83</td>
<td>Ocasis cordulata</td>
<td>Herb</td>
<td>Leaf, Whole plant</td>
</tr>
<tr>
<td>84</td>
<td>Pheobe lansedolata</td>
<td>Tree</td>
<td>Berries</td>
</tr>
<tr>
<td>85</td>
<td>Picea smithiana</td>
<td>Tree</td>
<td>Resin</td>
</tr>
<tr>
<td>86</td>
<td>Pinus roxburghii</td>
<td>Tree</td>
<td>Resin</td>
</tr>
<tr>
<td>87</td>
<td>Plantago major</td>
<td>Herb</td>
<td>Whole plant, Seed</td>
</tr>
<tr>
<td>88</td>
<td>Podophyllum hexandrum</td>
<td>Herb</td>
<td>Rhizome, Fruit</td>
</tr>
<tr>
<td>No</td>
<td>Species</td>
<td>Habit</td>
<td>Plant part used</td>
</tr>
<tr>
<td>----</td>
<td>---------------------------------</td>
<td>-------------</td>
<td>-----------------------------</td>
</tr>
<tr>
<td>89</td>
<td>Polygonum amplexicaule</td>
<td>Herb</td>
<td>Root</td>
</tr>
<tr>
<td>90</td>
<td>Polygonum nepalense</td>
<td>Herb</td>
<td>Whole plant</td>
</tr>
<tr>
<td>91</td>
<td>Potentilla atrosparginea</td>
<td>Herb</td>
<td>Leaf</td>
</tr>
<tr>
<td>92</td>
<td>Principia utilis</td>
<td>Shrub</td>
<td>Seed, Fruit</td>
</tr>
<tr>
<td>93</td>
<td>Punica granatum</td>
<td>Shrub</td>
<td>Root, Stem, Fruit</td>
</tr>
<tr>
<td>94</td>
<td>Pupalia lappacea</td>
<td>U Shrub</td>
<td>Fruit</td>
</tr>
<tr>
<td>95</td>
<td>Quercus lechu-trichophora</td>
<td>Tree</td>
<td>Seed</td>
</tr>
<tr>
<td>96</td>
<td>Ranunculus arvensis</td>
<td>Herb</td>
<td>Leaf</td>
</tr>
<tr>
<td>97</td>
<td>Raphanus sativus</td>
<td>Herb</td>
<td>Leaf, Seed</td>
</tr>
<tr>
<td>98</td>
<td>Rheum australe</td>
<td>Herb</td>
<td>Root</td>
</tr>
<tr>
<td>99</td>
<td>Rheum veebliaum</td>
<td>Tree</td>
<td>Leaf</td>
</tr>
<tr>
<td>100</td>
<td>Rhododendron arboetum</td>
<td>Shrub</td>
<td>Root, Leaf</td>
</tr>
<tr>
<td>101</td>
<td>Rhododendron campanulatum</td>
<td>Shrub</td>
<td>Root, Leaf</td>
</tr>
<tr>
<td>102</td>
<td>Rizinus communis</td>
<td>Shrub</td>
<td>Seed, Leaf</td>
</tr>
<tr>
<td>103</td>
<td>Rumex hastatus</td>
<td>Herb</td>
<td>Leaf</td>
</tr>
<tr>
<td>104</td>
<td>Rumex nepalensis</td>
<td>Herb</td>
<td>Leaf</td>
</tr>
<tr>
<td>105</td>
<td>Saussurea costus</td>
<td>Herb</td>
<td>Root</td>
</tr>
<tr>
<td>106</td>
<td>Saussurea obvallata</td>
<td>Herb</td>
<td>Root</td>
</tr>
<tr>
<td>107</td>
<td>Senecio lacteis</td>
<td>Herb</td>
<td>Leaf</td>
</tr>
<tr>
<td>108</td>
<td>Shorea robusta</td>
<td>Tree</td>
<td>Seed, Fruit</td>
</tr>
<tr>
<td>109</td>
<td>Siegesbeckia orientalis</td>
<td>Herb</td>
<td>Whole plant</td>
</tr>
<tr>
<td>110</td>
<td>Skimmia laureola</td>
<td>Shrub</td>
<td>Leaf</td>
</tr>
</tbody>
</table>

## Table 2: Dermatological problems and plant species used to cure these skin problems by local people of Uttarakhand

<table>
<thead>
<tr>
<th>Dermatological problems</th>
<th>No of species</th>
<th>Species</th>
</tr>
</thead>
<tbody>
<tr>
<td>Goiter</td>
<td>1</td>
<td>Solanum nigrum</td>
</tr>
<tr>
<td>Frost bite</td>
<td>2</td>
<td>Juglans regia, Solanum tuberosum</td>
</tr>
<tr>
<td>Lice</td>
<td>3</td>
<td>Acorus calamus, Ageretum corniozeides, Cuscuta reflexa</td>
</tr>
<tr>
<td>Bruises</td>
<td>3</td>
<td>Codonopsis ovata, Geranium himalayense, Saussurea obvallata</td>
</tr>
<tr>
<td>Gout</td>
<td>3</td>
<td>Gloriosa superb, Melia azedarach, Verbascum thapsus</td>
</tr>
<tr>
<td>Pimples</td>
<td>4</td>
<td>Butea monosperma, Punica granatum, Syzygium cuminti, Celtis australis</td>
</tr>
<tr>
<td>Carbuncle</td>
<td>6</td>
<td>Albezia lebeck, Anogeissus latifolia, Cynodon dactylon, Ficus religiosa, Shorea robusta, Woodfordia fruticosa</td>
</tr>
<tr>
<td>Blisters</td>
<td>7</td>
<td>Allium cepa, Ficus bengalensis, Ficus recemosus, Ficus religiosa, Syzygium cuminti, Taraxacum off, Vitex negundo</td>
</tr>
<tr>
<td>Itching</td>
<td>7</td>
<td>Allium cepa, Carissa carandas, Cassiope fastigiata, Cuscuta reflexa, Lantana camera, Vitex negundo, Zanthoxylum armatum</td>
</tr>
<tr>
<td>Small pox</td>
<td>8</td>
<td>Azadirachta indica, Ficus racemos, Ficus religiosa, Nardostachys jatamasi, Shorea robusta, Skimmia laureola, Woodfordia fruticosa, Zanthoxylum armatum</td>
</tr>
<tr>
<td>Burns</td>
<td>11</td>
<td>Ageretum corniozeides, Ajuga bractacea, Bergenia ligulata, Euphorbba royleana, Frullialia roylei, Plantago major, Principia utilis, Ricinus communis, Shorea robusta, Waldhemia glabra, Woodfordia fruticosa</td>
</tr>
<tr>
<td>Eczema</td>
<td>12</td>
<td>Allium sativum, Arisaema flavum, Centauria iberica, Centella asiatica, Euphorbia hirta, Ranunculas arvensis, Tectona grandis, Terminalis chebula, Thalictrum foliosulom, Vitex negundo, Zanthoxylum armatum</td>
</tr>
<tr>
<td>Septic wounds</td>
<td>13</td>
<td>Ageretum corniozeides, Arnebia benthamii, Artemisia maritima, Azadirachta indica, Cuscuta capitata, Gaultheria mummularoides, Jurinea dolomiae, Melia azedarach, Mentha longifolia, Skimmia laureola, Toona ciliata, Urtica dioica, Viola biflora</td>
</tr>
<tr>
<td>Leprosy</td>
<td>15</td>
<td>Aconitum atrox, Ageretum corniozeides, Argemone mexicana, Atragalas himalayanus, Azadiracta indica, Bauhinia variegata, Centella asiatica, Corydalis meifolia, Ficus racemos, Stellaria media, Swertia chirayita, Pinus roxburgii, Ocimum sanctum, Gloriosa superb, Vitex negundo</td>
</tr>
<tr>
<td>Scabies</td>
<td>15</td>
<td>Ageretum corniozeides, Argemone mexicana, Azadirachta indica, Euphorbba hirta, Ficus bengalensis, Ficus racemos, Ficus religiosa, Gloriosa superb, Quercus lechu-trichophora, Skimmia laureola, Swertia chirayita, Vitex negundo, Ziziphus officinale, Neolitsea pallens, Clematis barbella</td>
</tr>
<tr>
<td>Swelling</td>
<td>17</td>
<td>Achillea millefolium, Aconitum atrox, Ageretum corniozeides, Albezia lebeck, Codonopsis ovata, Cuscuta reflexa, Delphinium cashmerianum, Pinus roxburgii, Polygonum nepalens, Rheum australe, Ricinus communis, Rumex nepalensis, Solanum nigrum, Taxus baccata, Urtica dioica, Vitex negundo, Cocculus hirsutus</td>
</tr>
<tr>
<td>Boils</td>
<td>21</td>
<td>Ageretum corniozeides, Ajuga bractacea, Albezia lebeck, Argemone mexicana, Azadirachta indica, Berberis aristata, Euphorbia hirta, Allium cepa, Butea monosperma, Lyonia ovalifolia, Mentha longifolia, Pinus roxburgii, Rheum webbianum, Rhododendron campanulatum, Ricinus communis, Siegesbeckia orientalis, Skimmia laureola, Solanum nigrum, Thalictrum foliosulom, Urtica dioica, Vitex negundo</td>
</tr>
</tbody>
</table>
Influence of arbuscular mycorrhizal fungi on andrographolide concentration in *Andrographis paniculata*

*Aust J Medical Herbalism* 23:1;34-6

The following tables were inadvertently omitted from the above article published in March 2011. Figures for this article can be downloaded from www.nhaa.org.au/Publications/AJMH/downloads.

Table 1: Plant dry weight and shoot dry weight in *A. paniculata* inoculated with different treatments and control

<table>
<thead>
<tr>
<th>Sr. No.</th>
<th>Treatments</th>
<th>Shoot dry wt. (g)</th>
<th>Plant dry wt. (g)</th>
<th>Number of leaves/plant</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Sterilized (Control) (C1)</td>
<td>0.10 ± 0.05</td>
<td>0.20 ± 0.01</td>
<td>6.60 ± 2.30</td>
</tr>
<tr>
<td>2</td>
<td>Unsterilized (Control) (C2)</td>
<td>0.90 ± 0.08</td>
<td>1.00 ± 0.02</td>
<td>13.66 ± 2.08</td>
</tr>
<tr>
<td>3</td>
<td><em>Acaulospora scrobiculata</em> (M2)</td>
<td>0.35 ± 0.02</td>
<td>0.36 ± 0.06</td>
<td>12.00 ± 3.46</td>
</tr>
<tr>
<td>4</td>
<td><em>Gigaspora albida</em> (M4)</td>
<td>0.54 ± 0.05</td>
<td>0.59 ± 0.08</td>
<td>37.30 ± 4.60</td>
</tr>
<tr>
<td>5</td>
<td><em>Scutellospora calospora</em> (M1)</td>
<td>0.18 ± 0.02</td>
<td>0.21 ± 0.05</td>
<td>17.33 ± 1.10</td>
</tr>
<tr>
<td>6</td>
<td><em>Globostrum fasciculatum</em> (M3)</td>
<td>0.25 ± 0.06</td>
<td>0.28 ± 0.09</td>
<td>18.00 ± 4.00</td>
</tr>
<tr>
<td>7</td>
<td><em>Scutellospora biornata</em> (M5)</td>
<td>0.22 ± 0.01</td>
<td>0.26 ± 0.07</td>
<td>14.00 ± 2.00</td>
</tr>
</tbody>
</table>

Values are mean of 3 replicates. Columns with different letters indicate that treatments were significantly different at 5% level of significance (P≤0.05).

Table 2 (with 3): Percentage of andrographolide concentration and total andrographolide content per plant in treatments and control

<table>
<thead>
<tr>
<th>Treatments</th>
<th>Retention time</th>
<th>Andrographolide concentration (%)</th>
<th>Total andrographolide content per plant (mg/plant)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sterilized (Control)</td>
<td>15.0</td>
<td>1.98</td>
<td>0.198</td>
</tr>
<tr>
<td>Unsterilized (Control)</td>
<td>15.1</td>
<td>5.78</td>
<td>5.2</td>
</tr>
<tr>
<td><em>A. scrobiculata</em></td>
<td>15.3</td>
<td>14.6</td>
<td>3.21</td>
</tr>
<tr>
<td><em>Gl. albida</em></td>
<td>15.4</td>
<td>58.53</td>
<td>31.6</td>
</tr>
<tr>
<td><em>S. calospora</em></td>
<td>15.3</td>
<td>8.06</td>
<td>1.44</td>
</tr>
<tr>
<td><em>G. fasciculatum</em></td>
<td>15.4</td>
<td>8.06</td>
<td>2.01</td>
</tr>
<tr>
<td><em>S. biornata</em></td>
<td>15.3</td>
<td>13.8</td>
<td>4.83</td>
</tr>
</tbody>
</table>
Are your patient’s
STRESSED?

NeuroCalm

Each tablet contains:
Extracts equivalent to:
Zizyphus spinosa (Zizyphus), seed dry 3000 mg
Magnolia officinalis (Magnolia), bark dry 1500 mg
Pueraria labata (Pueraria), root dry 2000 mg
Passiflora incarnata (Passionflower), herb dry 1300 mg

NeuroCalm is a herbal supplement specifically designed for the promotion of a healthy stress response in men and women of all ages.

Clinical Benefits
May assist in relieving nervous tension and anxiety.
Promotes quiet, restful sleep.
For relief of muscular tension due to stress and anxiety.

This combination of traditional Chinese and Western herbs may assist in calming patients who are exhibiting symptoms of anxiety and tension during times of stress.


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Helicobacter pylori infection: a review of current scientific research on the efficacy or potential of herbal medicine for the treatment of H. pylori infection of the gastric mucosa

Lee Williams
Currently completing an Advanced Diploma of Western Herbal Medicine at Nature Care College Sydney
Email willeeams@yahoo.com.au

Objective: To conduct a review of the current scientific literature on the efficacy of herbs in the treatment and eradication of Helicobacter pylori infection in the gastric mucosa.

Methods: Research for scientific articles was obtained primarily through Medline and Google Scholar. A total of 53 scientific articles were examined, the vast majority of which were in vitro studies. Only one double blind randomised controlled study was identified involving the use of cranberry. Two controlled trials using garlic were also included.

Results: Helicobacter pylori infection of the gastric mucosa is prevalent throughout the world, especially in countries of poor socioeconomic background. Infection has been proven to be a risk factor for the development of peptic ulcers, gastritis and in some cases adenocarcinoma or lymphoma. Eradication of the bacterial infection and treatment of symptoms due to infection are primarily treated with two antibiotics and a proton pump inhibitor however bacterial resistance to antibiotic therapy is now becoming a problem. A safe and cheap alternative treatment for this widespread infection is being sought.

Current research shows that the use of herbs and herbal extracts for the treatment of Helicobacter pylori infection of the gastric mucosa has great potential. Unfortunately the majority of studies are in vitro with minimal in vivo studies currently being conducted. The most promising and most researched herbs for the treatment of H. pylori infection include cranberry and garlic. Garlic demonstrates strong antibacterial and antiadhesive actions against H. pylori and appears to have a synergistic action when used in conjunction with current orthodox antibiotic therapy. Cranberry inhibits H. pylori infection by preventing adhesion of the bacteria to the gastric mucosa and by acting as a bacteriostatic. Synergism between cranberry and antibiotic therapy with a proton pump inhibitor has been demonstrated. Licorice, green tea, cinnamon, chilli and numerous culinary herbs also demonstrate significant antibacterial or antiadhesive actions. Alcoholic extracts of herbs for the treatment of H. pylori infection appear to be most effective. With regard to herbal treatment, issues that need to be resolved with in vivo studies are herb extraction method, dosage, method of administration and length of time of treatment.

Introduction

Helicobacter pylori is a common bacterium that infects the stomachs of approximately 50% of the world population (Go 2002). Australian physicians Warren and Marshall discovered the unidentified bacteria in the early 1980s in the gastric mucosa and duodenum of patients suffering from peptic ulceration (Gaby 2001). It is now accepted that Helicobacter pylori infection is a precursor to chronic gastritis, peptic and duodenal ulceration (Gaby 2001). Where gastric inflammation persists for decades, atrophic gastritis can evolve into adenocarcinoma or increase the person’s risk of developing mucosa associated lymphoid tissue (MALT) lymphomas (Evans 2000, Guruge 1998). From 30-90% of gastric carcinomas are attributable to Helicobacter pylori infection (Guruge 1998). In countries such as Japan where the incidence of gastric cancer is high, the infection rate of Helicobacter pylori has also been found to be high (Go 2002). Helicobacter pylori infection is hypothesised to play a role in cardiovascular disease in some people however clear evidence is yet to be uncovered (Gasbarrini 1999, Martinez-Torres 2002).

Transmission of the bacterium is primarily through compromised water sources but also occurs through person to person transmission (Go 2002). A reduced incidence of infection has been observed in developed countries compared with underdeveloped nations where the carriage rates of infection are as high as 90% however the infection remains prevalent throughout the world (Go 2002, Sivam 1997).

Helicobacter pylori is a gram negative curved rod bacterium (Nostro 2005). H. pylori survives in the acid environment of the stomach by releasing the enzyme urease. Urease converts urea to ammonia, a strong base, which neutralises the acidity of the stomach, protecting the bacteria. The reduction in stomach acidity results in hypochlorhydria which may lead to a variety of gut disorders especially digestive disorders (Lin 2005). Ammonia generated by H. pylori causes damage to the gastric mucosa inducing gastritis and potentially leading to ulceration (Lin 2005).

The bacterium takes hold through adhesin host cell interactions between gastric epithelial cells and...
erythocytes (Burger 2002, Evans 200). As of 2002 approximately 10 different types of adhesins have been described however it is accepted that many other mechanisms of adhesion may be involved (Burger 2002). Upon infection, rapid reproduction of the bacterium occurs in the stomach causing gastritis and a reduction in gastric acid production (Guruge 1998). In the majority of people this gastritis inflammation associated with Helicobacter pylori infection will settle causing asymptomatic gastritis and normal acid production. This condition will persist indefinitely unless treated.

Orthodox treatment of Helicobacter pylori infection

Helicobacter pylori infection is primarily treated with two antibiotics such as clarithromycin and amoxicillin or metronidazole in conjunction with a proton pump inhibitor such as omeprazole (O’Mahony 2005). This regimen is called triple therapy. However the prevalence of antibiotic resistance has increased over the years resulting in a decrease in effectiveness of triple therapy (O’Mahony 2005). As a consequence new therapy regimes have been designed where four or five drugs are prescribed to combat the infection (O’Mahony 2005). Eradication of the bacterial infection is conclusive when there is no evidence of infection 4 weeks after treatment however reinfection is not uncommon occurring in approximately 20-40% of patients who have undergone triple therapy. Reinfection typically occurs 3-6 months after initial treatment (Gaby 2001, Wittschier 2009). At the present time orthodox treatment is the only therapy that has a proven record for eradicating H. pylori with a cure rate of up to 95% (where triple therapy is used) (Mahady 2005).

There is currently no viable, proven alternative to antibiotic therapy (Gaby 2001). Due to the rising incidence of antibiotic resistance, research into alternative solutions including plant based therapies, are now being investigated. Research on the effectiveness of herbal medicine in treating H. pylori infection has been primarily in vivo thus far. Positive in vitro results unfortunately do not necessarily mean that the herb will be successful in vivo and this is where current research information is severely deficient. The current focus of treatment, whether orthodox or herbal, is based on the antibiotic or antimicrobial properties of a herb or drug and its ability to prevent bacterial adhesion to gastric cells (O’Mahony 2005).

Methodology

The medical database Medline (1950 to present) and Google Scholar were used to identify research involving Helicobacter pylori and herbal medicine. Key words included Helicobacter pylori, herbal medicine, herbs, phytotherapy in combination. Specific herbs were also targeted including garlic, turmeric, cranberry, chilli, tea and licorice.

Review procedure

Relevant articles included in the review included in vivo and in vitro research involving herb or plant products effect against Helicobacter pylori specifically. References from recent research were investigated to obtain first hand information and results.

Results: specific herbal therapies

Cranberry, Vaccinium macrocarpon

As described, the primary method of infection by Helicobacter pylori is through the bacterium adherence to the gastric mucous cells and gastric epithelial cells underlying the mucous layer in the stomach. One of the primary directions of research is to find ways of preventing adhesion of the bacterium to the epithelial cells thus reducing infection rates. The consumption of cranberry (Vaccinium macrocarpon) juice daily has been proven to be effective in preventing adhesion of E. coli to the bladder wall, preventing or reducing the incidence of cystitis (Burger 2000). Howell et al (2005) suspect that A-type proanthocyanidins found in cranberry (as well as other berries), are the primary cause of anti-adhesion activity. A small in vitro study examining the effects of a proanthocyanidin isolated cranberry juice cocktail on adhesion of E. coli to the bladder wall demonstrated significant anti-adhesion activity. It is this mechanism of anti-adhesion that has been applied to H. pylori.

Research involving cranberry’s effects on preventing H. pylori adhesion are primarily in vivo. Burger et al (2002) demonstrated that there is significant inhibition of Helicobacter pylori adhesion to human gastric mucous when exposed to high molecular weight constituents of cranberry at 37°C. Cranberry juice also appears to inhibit sialic acid specific adhesion to gastric mucous, the mechanism of which is yet to be identified. Specific glycoprotein receptors known as fimbriae or lectins are found on the H. pylori wall surface that have the ability to specifically bind to sugars that are present on mucosal cell or epithelial cell walls. Large molecular weight sugars, such as those found in cranberry juice, have been shown to block these receptors preventing bacterium and cell adhesion (Vattem 2005).

The bacteriostatic actions of cranberry were identified by Matsushima et al (2008). The in vivo study using cranberry extract showed complete inhibition of H. pylori growth and proliferation. Inhibition of the bacterium was dose dependent. The researchers then focused on which constituent of cranberry was responsible for this bacteriostatic action and found that the polyphenol content was the primary inhibitor. Morphological analysis of the bacterium after exposure to cranberry identified a shape change in the bacterium from a curved rod to a coccooid form, thereby preventing its proliferation and normal function.

A double blind randomised placebo controlled trial conducted in China by Zhang et al (2005), assessing
the efficacy of cranberry juice in suppressing \textit{H. pylori} infection in 189 patients, found that the consumption of 250 mL of cranberry juice twice daily for 90 days was effective in treating 14\% of the patients when compared with the placebo group (p<0.05). Interestingly this data found that suppression of \textit{H. pylori} was clearly evident after 35 days of cranberry consumption with very little statistical difference beyond this time frame (i.e. between day 35 and day 90).

As well as presenting with bacteriostatic and anti-adhesive abilities, cranberry has also been found to be useful as an adjunct treatment for eradicating \textit{H. pylori} infection. Cranberry was found to improve the effectiveness of antibiotic triple therapy that includes the use of a proton pump inhibitor (Shmueli 2004, Shmueli 2007). Interestingly the benefits of using cranberry in conjunction with triple therapy appeared to be most effective in female patients. The reason why this should occur could not be explained. It was suggested that the interaction of the bacteria to female versus male epithelia may be different (Shmueli 2007).

As well as an adjunct to orthodox therapies, cranberry may be effective when used in conjunction with probiotics such as \textit{Lactobacillus johnsonii} La. A study by Gotteland et al (2008) suggested that cranberry when used in conjunction with the probiotic \textit{L. johnsonii} may be useful in treating asymptomatic \textit{H. pylori} infection by inhibiting the growth and proliferation of the bacteria. The researchers conducted their study using a pediatric population (ages 6-16 years). Minimal synergistic effects were observed when compared with the efficacy of each product individually. It is worth noting that cranberry did not appear to have a detrimental effect on the probiotic. The effect of cranberry on commensal gastric and gut bacteria has not been fully researched.

Synergy between cranberry and oregano (\textit{Origanum vulgare}) was demonstrated in an in vivo study conducted by Lin et al (2005). Researchers focused on urease inhibition of \textit{H. pylori} in agar diffusion. Significant inhibition of urease production was demonstrated when the two substances were used in conjunction. The mechanism of inhibition was not clearly identified however the combination of phenolics (found in both oregano and cranberry) at the bacteria cellular membrane were suspected to be strongly involved. When the inhibitory actions of each substance were examined individually, the extent of inhibition was significantly less. The most effective combination was found to be 25\% oregano to 75\% cranberry.

\textbf{Garlic (\textit{Allium sativum})}

Garlic has been used in the treatment of ailments for centuries. It has proven antimicrobial, antibiotic, antibacterial and immunostimulating properties (Braun 2005). Researchers investigated the efficacy of garlic as an antimicrobial in the eradication of \textit{H. pylori}. Difficulties with studying the role of garlic have arisen due to the different varieties of garlic that are available, the composition of the garlic used, the form in which it is utilised and the amounts or dosages used for consumption or investigation being all so variable that evaluation and reproducibility of research results is difficult (Sivam 2001). Despite these issues some interesting facts have already been identified. Firstly the incidence of stomach cancer (which is now known to be primarily due to \textit{H. pylori} infection) is low in populations with a high consumption of garlic and other \textit{Allium} vegetables such as onions (Sivam 2001). Secondly the antibiotic action of garlic (suspected to be due to its thiosulfinate content) has not resulted in the development of bacterial resistance which is not the case with current antibiotic therapies (Sivam 2001).

Garlic oil has been researched as a treatment for \textit{H. pylori} and appears to be promising in the in vivo setting (O’Gara 2000, 2008, Ohta 1999). However garlic oil was found to be most effective in a high acid environment, a condition that may be lacking in the stomachs of infected persons (O’Gara 2008). Reduced acidity is apparent when food and drink is in the stomach, hence the effectiveness of garlic oil was found to be reduced in an in vitro experiment where the efficacy of garlic oil was tested in a replicated, non fasted environment (O’Gara 2008). Therefore in vivo investigation of the efficacy of garlic oil needs to be performed in both the fasting and non fasting patient. The dosage of garlic oil also needs to be defined.

A small study containing 5 patients examined the effectiveness of steam distilled garlic oil in the suppression of \textit{H. pylori}. The patients were given 4 mg of garlic oil with each meal over a 14 day period. No beneficial effect was identified (McNulty 2001). An additional study using 15 female patients found no benefit when using garlic oil standardised to 800 \(\mu\)g of allicin over a two week period (Aydin 2000).

A randomised factorial controlled trial using aqueous ethanol garlic extract (400 mg) and steam distilled garlic oil (2 mg twice daily) over a 7.3 year period yielded negative results where there was no evidence of \textit{H. pylori} suppression or eradication. The results were compared with a 2 week course of antibiotics which produced positive results. The study did not identify any synergistic action between garlic and the antibiotics prescribed (Gail 2007).

Inhibition of \textit{H. pylori} by garlic appears to relate to its thiosulfinate content. Approximately 40 \(\mu\)g/mL of thiosulfinate has been shown to exert significant inhibitory effects upon \textit{H. pylori} which equates to approximately 5 g (2 small cloves) of fresh garlic (Sivam 1997). The researchers of this study suggest that this is effective in a non fasted stomach and that for efficacy, the consumption of garlic needs to be maintained for long periods (not specified). This may explain why in populations which have a high and constant intake...
of garlic in their diets there is a lower incidence of \textit{H. pylori} infection (Sivam 1997). Additional research has demonstrated a lack of synergy or antagonism between garlic and antibiotics however the study did uncover a synergistic action between omeprazole (proton pump inhibitor) and garlic (Cellini 1996, Jonkers 1999). The researchers recommended further investigation.

\textbf{Chilli, cayenne (\textit{Capsicum frutescens})}

Capsaicin is the active ingredient in chilli which is responsible for the inhibition of pro-inflammatory cytokines and chilli’s cytoprotective actions (Lee 2007). Capsaicin has been found to be effective in inhibiting \textit{H. pylori} induced inflammation by inhibiting the release of interleukin-8 which is produced by infected gastric cells (Lee 2007). Capsaicin inhibits the growth of \textit{H. pylori} (in vitro) in a time and concentration dependent manner with maximum bactericidal activity occurring in less than 4 hours (Jones 1997). The maximum inhibitory concentration (MIC) was found to be approximately 1 mg/mL which is easily achievable in a population that consumes a high volume of chilli (Jones 1997). It is recognised however that increased chilli consumption is potentially detrimental to the gastric mucosa due to the promotion of gastric epithelial cell exfoliation following chilli consumption. High chilli consumption is considered a causative factor in gastric cancer development and is independent of \textit{H. pylori} infection (Lopez-Carillo 2003).

\textbf{Tea (\textit{Camellia sinensis})}

The consumption of tea on a regular basis has also been assessed as a protective factor against \textit{H. pylori} infection. Yee et al (2002) found a significant inverse relationship between \textit{H. pylori} infection and tea consumption. The active constituents were considered to be the catechin components of tea such as epigallocatechin (EGC), epicatechin (EC), epitechin gallate (ECG) and epigallocatechin gallate (EGCG). Catechins act on bacterial membranes and inhibit urease activity of \textit{H. pylori} in vitro (Matsubara 2003, Yee 2000, Yee 2002). The type of tea could not be defined as the study was retrospective and many types of Chinese tea were consumed by the test subjects on a random basis. In vitro studies of tea on \textit{H. pylori} failed to conclude whether or not tea can eradicate \textit{H. pylori} or only induce suppression (Yee 2000). Research conducted by Lee et al (2006) suggests that tea may act as a bacterial anti-adhesion agent against \textit{H. pylori}.

\textbf{Licorice (\textit{Glycyrrhiza glabra})}

Licorice is another herb traditionally used for the treatment of peptic ulcers (Braun 2005). Strong anti-adhesive and mild cytotoxic effects against \textit{H. pylori} were demonstrated using an aqueous extract of licorice (Wittschier 2009). Specific flavonoids extracted from \textit{Glycyrrhiza} species such as glycyrrhetinic acid were found to exhibit significant antibacterial properties against \textit{H. pylori} as well as clarithromycin and amoxicillin resistant strains of \textit{H. pylori} (Fukai 2002, Krausse 2004). These results have prompted the proposition that licorice extracts may be useful in preventing reinfection after prior triple therapy (Fukai 2002).

\textbf{Herbal medicine}

Many herbal extracts have been researched for their in vitro antimicrobial and antibacterial properties against bacteria such as \textit{H. pylori}. Unfortunately very few in vivo studies have been conducted. Well designed clinical trials involving large numbers of patients are required to provide proof of efficacy which, despite promising in vivo results, have not been conducted (Martin 2003).

Nostro et al (2005) conducted an in vitro study on the efficacy of 17 herbs for their antibacterial activity against \textit{Helicobacter pylori}. Ethanolic and aqueous extracts of each herb were obtained and examined against the bacterium. The results concluded that the aqueous extracts of globe artichoke (\textit{Cynara scolymus}) and oregano (\textit{Origanum vulgare}) demonstrated the most potent inhibition of \textit{H. pylori}. Of the ethanol extracted herbs, \textit{Cynara scolymus} and ginger (\textit{Zingiber officinalis}) were the most effective at inhibiting \textit{H. pylori}. Overall the ethanol extracts exhibited stronger antibacterial properties compared with the aqueous extracts. The authors presumed this to be due to the higher amounts of bioactive compounds extracted by ethanol compared with water. This information may have implications for future in vivo study designs.

O’Mahony et al (2005) evaluated common culinary herbs such as garlic, turmeric, chilli, ginger, cumin, cinnamon, borage, oregano, black caraway, sage, tarragon, nutmeg, dill, black pepper, coriander, fenugreek, tea, Bengal quince and nightshade for their ability to inhibit adhesion or inhibit growth of \textit{H. pylori}. The herbs were boiled in water to simulate the cooking process and these individual extracts were assessed against the \textit{H. pylori} bacterium. The extracts of turmeric (\textit{Curcuma longa}), borage (\textit{Borago officinalis}) and parsley (\textit{Petroselinum crispum}) were found to be the most effective inhibitors of \textit{H. pylori}. As for effective antibacterial properties, cumin (\textit{Cuminum cyminum}), ginger (\textit{Zingiber officinalis}), chilli (\textit{Capsicum frutescens}) and turmeric (\textit{Curcuma longa}) were found to be the most efficient. It was suspected that heat associated with the boiling of garlic reduced its antibacterial qualities.

Previous research has proven that the thiosulfinolate content of garlic is negatively affected by high heat and it is the thiosulfinolate content that is responsible for the antibacterial properties of garlic (Canizares 2004, Cellini 1996, Jonkers 1999).

By using a methanolic extraction of herbs, Mahady et al (2005) found that fennel (\textit{Foeniculum vulgare}), ginger (\textit{Zingiber officinalis}), marjoram (\textit{Origanum majorana}), nutmeg (\textit{Myristica fragrans}), passionflower (\textit{Passiflora incarnata}), rosemary (\textit{Rosmarinus officinalis}), turmeric
**Comments and conclusion**

There have been numerous in vitro studies examining the effect of herbs and herbal extracts on *Helicobacter pylori*, many of which have proven antibacterial, anti-adhesive and gastroprotective effects. There has been a paucity of in vitro studies and those that have been conducted often contain very small numbers. Overall the most researched and at this time the most promising herbs that could be used for the treatment of *Helicobacter pylori* infection include garlic, cranberry and oregano in combination with cranberry, chilli, Chinese tea, turmeric and licorice. Many culinary herbs also appear to be beneficial which interestingly have been used traditionally for the treatment of gastric and gut disorders for thousands of years.

There are many factors that need to be decided before an effective in vivo study can be conducted on a herb, some of which have been addressed in several of the presented research papers. Probably the most important factor is the preparation of the herb. As noted by several authors, ethanolic or alcoholic extracts appear to be the most potent in inhibiting or eradicating *H. pylori* compared with aqueous extracts however both often displayed effectiveness against the bacteria. Heat may be detrimental to some of the active constituents of other herbs. Identification of the active constituent and ensuring it has been extracted sufficiently may be another factor in study design. Other obvious issues include dosage, the part of the plant used, the duration of use, fasting versus non fasting before ingestion of the herb or supplement and frequency of dosage.

At this point in time current research has proven the bactericidal nature of many herbs in an in vitro setting as well as other actions against *H. pylori* such as anti-adhesive abilities and the inhibition of bacterial urease production. What is now required are substantial, large scale, well designed in vivo studies to confirm the efficacy of herbal medicines against *Helicobacter pylori* infection.

A summary of research for the treatment of *H. pylori* infection using herbal preparations can be found on www.nhaa.org.au under Publications/AJMH/downloads.

**References**


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Reviews of articles on medicinal herbs

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These abstracts are brief summaries of articles which have appeared in recent issues of herbal medicine journals, many of which are held in the NHAA library.

Value of Panax in stroke treatment


Ischaemic stroke is one of the major killers in most countries and is the leading cause of long term disability in survivors. Conventional pharmaceutical approaches target mechanisms occurring in acute stroke with drugs such as antithrombosics and thrombolytics. The problem is that these can only be given to selected patients. Neuroprotective therapy is also used with the aim of reducing the effects of ischaemia, however evidence of its efficacy is lacking.

Panax notoginseng is one of the main herbs in Sanchi, one of the most widely used herbal medicines in China for this type of stroke. The main active ingredients are saponins which have been isolated and used in clinical trials of ischemic stroke in China with positive results.

This randomised double blind clinical trial examined the efficacy of Sanchitongshu, an agent of Sanchi containing Panax notoginseng, with a higher purity of panaxatriol saponins (PTS) and Rg1 (which has the strongest antiplatelet activity of all the PNS). The herbal medicine was given with aspirin 50 mg daily (in comparison with aspirin alone) in the treatment of patients with light and moderate ischemic stroke of anterior cerebral circulation in acute and subacute stages. The dose of Sanchitongshu was 200 mg three times daily (standardised to ginsenoside Rg1 50%, ginsenoside Re 6%, notoginsenoside R1 11%).

One hundred and forty patients completed the four week trial, with equal distribution between males and females. Post treatment neurological function, as measured by the European Stroke Scale (ESS), was significantly improved in both groups. However significantly more of those taking both Sanchitongshu and aspirin achieved marked recovery and improvement after treatment, especially with regards to movement of the limbs. Activities of daily living were significantly improved in both groups, again more so in the Sanchitongshu arm. No significant adverse effects were noted during the trial.

Overall this extract of Panax notoginseng demonstrated significant adjuvant antiplatelet activity with aspirin in acute and subacute ischemic stroke. The clinical improvements were superior in the combination group compared with those taking aspirin alone.

Using birch bark for chronic hepatitis C


Chronic hepatitis (types B and C) is a disease which affects somewhere between 400 and 500 million people worldwide and is characterised by significant levels of morbidity and mortality. Pharmaceutical treatment of hepatitis C virus (HCV) successfully eradicates the virus in 60% of people, but a significant number do not respond. Thus there is a need for other effective treatments for the condition. The bark of Betula alba L, birch, has been used in traditional healing by Native Americans and Russians for many years. Modern pharmacological studies have shown the birch triterpenes to have antiallergic, antiviral, antimicrobial, hepatoprotective and antitumor properties. Murine studies of HCV have also displayed hepatoprotective benefits from treatment with this plant, and it has been shown to lower elevated liver enzymes in rats with alcoholic liver disease. This makes birch an exciting potential treatment for chronic types of hepatitis.

In the current pilot study 42 patients with serologically confirmed chronic hepatitis C were treated for 12 weeks with 160 mg of birch bark extract (BBE) (standardised to 75% betulin and 3.5% betulinic acid) per day. The primary outcome parameter measured was the rate of alanine aminotransferase (ALT) normalisation. A number of other parameters were also assessed. Those enrolled in the study all had ALT readings of at least 1.5-fold above the upper limit of normal for at least four months prior to start of the study. Dosage of the BBE was 20 mg capsules eight times a day (two in the morning, three before lunch, and three in the evening) for 90 days.

After the 12 week trial period the level of ALT was decreased in 54% of participants and normalised (p=0.046). HCV RNA, a viral marker, was significantly reduced in 43.2% (p=0.016) of people. Subjective symptomatology also improved. Reports of fatigue and abdominal discomfort were reduced by 6-fold (p=0.028) and 3-fold (p=0.05) respectively and there were significant reductions in dyspepsia from baseline. Researchers suggest that the potent antioxidant activity of betuin may be at least partially responsible for these effects.

As a pilot trial this is promising but further controlled clinical trials are necessary to more fully appreciate the clinical relevance of the findings.
Reduce skin ageing with gotu kola?


Centella asiatica, commonly known as gotu kola, is an Ayurvedic herb with long standing traditional use in treatment of fevers, bacterial infections, venous insufficiency, mental disorders and skin diseases. Recently this plant has been included in cosmetic preparations for cellulite.

The major known bioactive constituents of the plant include polyacetylenes, triterpenoid saponins (asiaticoside and madecassoside) and saponogens. Given the large demand for these, researchers have in the past attempted to overproduce them in laboratories using in vitro culture techniques. Recently researchers attempting to do just that were surprised to find low amounts of these phytochemicals in their products but rather large amounts of caffeoyl derivatives, in particular a product called 3,5-O-dicafeoyl-4-omalonilquinic acid (renamed irbic acid, for ease of discussion). A major activity of this phytochemical is its strong ability to absorb UV light, particularly in the range of 300 and 330 nm.

This acid has never been identified in gotu kola before leading to the scientists conducting research into its other properties. Irbic acid was found to have a strong free radical scavenging ability and a significant inhibitory influence on collagenase (the enzyme responsible for the degradation of the collagen matrix) activity.

The fact that the molecule helps to protect the skin from UV damage and inhibits collagen breakdown, in addition to its small size and hydrophobicity suggest the possible utilisation of the substance as a topical agent to assist in reducing skin ageing.

The value of curcumin for gastric ulceration


Curcumin is one of the most well researched bioactive constituents of the spice turmeric (Curcuma longa). It has been shown to have gastroprotective properties, including an anti-inflammatory, vulnerary and chemopreventative actions. This recent study examined the role curcumin played on gastric acid secretion in murine models, in addition to its effects on acute gastric lesions. In rats with a gastric fistula or acute gastric damage curcumin was shown to be biologically active.

In the rats with fistula, doses of 1–200 mg/kg of curcumin decreased gastric acid secretion in a dose dependant manner. These same doses also significantly attenuated gastric damage induced by high doses of ethanol and water and restraint stresses. These effects were accompanied by increases in PGE2 generation and plasma gastrin levels.

If the rats were given the drugs indomethacin, celecoxib and capsazepine this significantly reduced the effects of the curcumin. On the other hand giving PGE2, L-arginine or CGRP then restored the hyperemic and protective effects conveyed by the spice.

Overall curcumin provides gastroprotection against induced gastric ulceration possibly via an antisecretory and antioxidising activity and the flow on effects of this (including PG/NO system activation, NFκB suppression, reduced lipid peroxidation and increased gastrin).

Effective herbal treatment for rheumatoid arthritis


Lei gong teng or thunder god vine are the traditional Chinese names for extracts of the flowers, leaves and roots of Tripterygium wilfordii Hook F (TWFH). In TCM this plant has been used for centuries in the treatment of rheumatoid arthritis. Three diterpinoids in the plant, triptolide, tripdiolide and triptonide have been attributed with the major anti-inflammatory properties responsible for the effect of this traditional medicine.

A study in America compared the efficacy of 60 mg three times daily of TWFH extract with sulfasalazine 1 g twice daily over 24 weeks. Whilst patients were allowed to continue their oral nonsteroidal anti-inflammatory drugs or prednisone, all disease modifying antirheumatic drugs were stopped 24 days prior to beginning the trial.

Overall 62 patients completed this randomised controlled trial which equated to 62% of the herbal group and 41% of the pharmaceutical group. Researchers then assessed the rate of achievement of 20% improvements in the American College of Rheumatology criteria (ACR 20). Secondary outcomes of radiographic scores of joint damage and serum levels of interleukin-6, cholesterol, cortisol, adrenocorticotropic hormone and safety were also assessed.

The group receiving TWFH extract had double the results of the sulfasalazine group with 65% compared with 32.8% achieving a 20% improvement in ACR 20 criteria. Results were similar for the ACR 50 and ACR 70, indicating significant improvement. Interleukin 6 levels rapidly and significantly decreased in the TWFH group and there was a lower radiographic progression of the disease (although not statistically significant). Adverse effect frequency was similar for both groups.
with patients reporting one adverse effect on average (mostly gastrointestinal symptoms which resolved). The patients taking the pharmaceutical therapy had a higher rate of adverse effects classified as moderate to severe by investigators.

This trial was reported in the Annals of Internal Medicine, a well known peer reviewed journal, which makes it more broadly available to practitioners of Western medicine. This was attributed to the fact that the study was well designed, rigorous and demonstrated significant results.

**Anticancer potential of ginger**


Ginger, Zingiber officinale, is a widely used therapeutic food and herb. It has been used across India, China and Arabic countries for treating many ailments including headaches, colds, fever, nausea and rheumatic conditions. How the plant is prepared is undoubtedly important in the therapeutic activity however few studies have examined this to date.

Ginger is known to have pronounced antioxidant, anti-inflammatory, antiemetic, anti-diabetic and anticancer properties, many related to the diarylheptanoids and gingerol related compounds. Most research focuses on fresh or dried ginger however steaming the root may affect its phytochemical make up and properties as occurs with other herbs such as ginseng root.

In this trial researchers steamed the ginger root at different temperatures for different times (100°C for 1 h or 120°C for 0.5, 1, 2, 4 and 6 h) then air dried the product. The constituents and antiproliferative effect of the fresh, dried and steamed gingers were then quantitatively compared. After the processing 15, 21 and 22 constituents were identified in the fresh, dried and steamed ginger (120°C 4 h) extract respectively. The researchers chose two of the more well known compounds to assess in each extract: gingerols (6-, 8- and 10-gingerol) and shogaol (6-shogaol). As a general rule the concentration of gingerols decreased with steaming but the level of 6-shogaol actually increased in a time dependant manner and reached the maximum quantity after 4 hr of steaming. Steaming at 120°C greatly increased the concentration of this compound compared with steaming at 100°C, suggesting that higher temperatures may be more beneficial for facilitating the conversion of shogaols from gingerols and producing more concentrated extracts. The level of 6-shogaol in steamed ginger at 120°C for 4 h was found to be approximately 7 and 12 fold higher than that in dried ginger and fresh ginger respectively.

When steamed extracts were compared with fresh and dried ginger they were also found to have more potent anticancer effects. In human Hela cancer cells proliferation assays exposed to ginger for 24 and 48 hours, the steamed ginger produced stronger anticancer effect than the fresh and dried extracts. This is likely due to the higher amounts of shogaol in the herb, as past studies have shown this to have stronger growth inhibitory effects than gingerols on A-549 human lung cancer cells, SK-OV-3 human ovarian cancer cells, SKMEL-2 human skin cancer cells and HCT-15 human colon cancer cells.

This study provides interesting food for thought on the best forms of ginger (and perhaps other herbs) to use in patients when seeking an anticancer effect.

**Antidepressant effects of Panax notoginseng**


The root of Panax notoginseng (PN), also known as tienchi, sangi or tianqi, is commonly used in traditional Chinese medicine for hemoptysis, hemostatic conditions and hematoma. The main active constituents are similar to those in Korean ginseng (Panax ginseng) and American ginseng (Panax quinquefolium), being the saponins ginsenosides and notoginsenosides.

Modern research has demonstrated a multiplicity of actions attributable to these compounds in tienchi ginseng including hypoglycemic, hypolipidemic, immunostimulatory, antitumor, anti-inflammatory, analgesic, antioxidant, hemostatic, antithrombotic, antiatherosclerotic, fibrinolytic, antiarrhythmic, hypotensive, estrogen like and even sperm motility enhancing effects.

In this present study researchers in China evaluated the efficacy of tienchi in murine models of depression. They used an extract of saponins from the caudexes and leaves of PN (SCLPN) containing high amounts of the ginsenosides Rb3, Rb1, Rc and the notoginsenoside Fc which are highly bioactive and usually found in lower amounts in extracts of the roots alone.

The scientists put the rats under chronic stress for three weeks. Those animals that exhibited signs of depression/anhedonia (tested via the sucrose preference test) were divided into three groups. These groups received either vehicle (n = 10), fluoxetine (1.8 mg/kg, n = 10) or SCLPN (70 mg/kg n = 12) once a day and remained under chronic stress for four weeks. Control groups received distilled water.

Following administration of the medications the rats were put through various tests and their responses examined. SCLPN seemed to exert antidepressant activities on the animals. Those receiving this extract demonstrated reduced immobility time in the forced swim test, reduced sucrose preference and reversed decreases in locomotor activity. Researchers attribute the effect to the particular mix of saponins in the extract.
Whilst the exact mechanism of action is uncertain, a number of experiments in the current study suggest that SCLPN exerted its antidepressant like effect by increasing the levels of serotonin, dopamine and noradrenaline. The animals treated with this extract showed increased head twitches similar to the positive control drug, indicating an increase in serotonergic activity in vivo. However this only held true at lower doses whilst higher doses resulted in fewer head twitches suggesting that the effects on the serotonergic system are more complex than previously thought. Other parts of the study showed that other mechanisms of action may include enhanced locomotor activity (via the dopaminergic system), inhibition of $[Ca^{2+}]$ elevations and increased expression of BDNF which plays a critical role in hippocampal neurogenesis.

This saponin containing extract of tienchi ginseng exerted antidepressant effects in murine models via a number of mechanisms including neurotransmitter modulation and neuroprotective effects.

**Antiallergic properties of lemon quince**


In the Western world there has been a rise in the rates of allergic diseases over the past few decades, particularly rhinitis and asthma. In part the initiation of allergic reactions (both early and late phase) is due to the release of soluble mediators of inflammation from basophilic cells, mast cells and nose and lung epithelial cells. In Europe around 30% of patients with allergic conditions use complementary therapies to manage them, mostly in order to avoid side effects.

One of the more commonly used products is Gencydo®, an aqueous quince extract (*Cydonia oblonga fructus* 1:2:1) combined with lemon juice (*Citrus limon* succus). This is based on a traditional medicine used in the area for centuries. In past trials this product has shown positive outcomes on grass pollen allergy and seasonal allergic rhinitis.

The aim of the present study was to analyse the effects of complementary medicine on the release of soluble mediators from basophilic cells, mast cells and lung epithelial cells in attempts to further clarify the mechanisms of action. Both human and murine cell lines were used to assess the effects on different body tissues.

Results demonstrated a Gencydo® induced inhibition of the release of soluble mediators from basophilic cells, mast cells and lung epithelial cells. In some areas the effects elicited were comparable to those of a number of pharmaceutical preparations used in treating asthma and allergic rhinitis including azelastine and dexamethasone. In addition to inhibition of degranulation of basophilic and mast cells, Gencydo® inhibited IgE mediated release of GM-CSF, a cytokine that promotes eosinophil activation and survival which may contribute to airway inflammation in asthma.

This data on mode of action suggests that Gencydo® may affect chronic allergic disorders beneficially via the inhibition of inflammatory and allergic mediator release.

**Hypolipidemic and antioxidant effects of notoginseng**


Sanchi is a traditional Chinese medicine prepared from the roots of *Panax notoginseng*. It is indicated for a number of cardiovascular conditions and is thought to increase coronary blood flow, reduce myocardial oxygen consumption, reduce bleeding, reduce blood pressure and counteract thrombus and excessive lipid peroxidation.

Cardiovascular disease (CVD) presents a major health burden worldwide and hyperlipidemia is a known risk factor for the development of these conditions including atherosclerosis. Free radical mediated peroxidation of polyunsaturated fatty acids of LDL and VLDL particles is proposed as a major contributor to the progression of atherosclerotic lesions. Agents that can lower blood lipid levels and prevent oxidation from occurring may help to reduce the preponderance of CVD within the community.

Researchers in China assessed the effects of sanchi on rats fed a diet of 10% pork fat (w/w) (on top of a basal diet containing 5 g fat/100 g) for four weeks. Experimental parameters included serum lipid levels, hepatic lipid peroxidation, levels of HMG-CoA reductase and antioxidant profiles. Rats were randomised to a control (normal diet) group, an untreated hyperlipidemic group (HL), hyperlipidemic animals with a high fat diet including 0.25% w/w sanchi powder (HLL), 0.5% w/w sanchi powder (HLM) and 1% w/w sanchi powder (HLH).

Compared with rats on a normal diet, those on a high fat diet weighed significantly more. Sanchi significantly attenuated this weight gain in the active groups. Administration of the herb at higher doses significantly reduced levels of LDL cholesterol, total cholesterol and triglycerides in hyperlipidemic rats. There was also an increase in levels of beneficial HDL cholesterol.

After 28 days of administration, hepatic HMG-CoA reductase levels were significantly elevated in the animals on a high fat diet. This was markedly reduced in those receiving Sanchi in the chow. The supplement also reduced levels of lipid peroxidation and increased the activity of antioxidant enzymes.

It appears that sanchi is likely to reduce the risk of coronary heart disease associated with oxidative stress and hyperlipidemia.
Reviews of medical journal articles

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These abstracts are brief summaries of articles in recent issues of medical journals. Articles selected are of a general nature for the information of practitioners of herbal medicine. A dominant theme is often present throughout the journals which will be reflected in the reviews.

Beetroot juice improves sports performance

Dietary nitrate supplementation has been shown to improve parameters in high intensity exercise. Previous studies have reported that dietary nitrate supplementation extended time to exhaustion during high intensity, constant work rate exercise by 15–25%; this can be estimated as an equivalent to improved sporting performance of approximately 1–2%.

The aim of this randomised double blind crossover study was to investigate the role of dietary nitrate supplementation (found in organic beetroot juice) on sports performance. Nine competitive male cyclists (mean ± SD: age 21 ± 4 yr, body mass 79.6 ± 9.7 kg, height 1.81 ± 0.08 m, VO2peak 56.0 ± 5.7 mL•kg−¹ •min−¹) participated in the study. All participants were trained non elite cyclists and none consumed dietary supplements.

The participants were required to report to the laboratory on at least five occasions during a 3 week period prior to the supplemented tests: completing a ramp incremental exercise test to determine VO2peak.

On test days participants had blood pressure measured (four times) and a venous blood sample (~4 mL) drawn. Samples were subsequently analysed for plasma (nitrite) and a venous blood sample (~4 mL) drawn. Samples were subsequently analysed for plasma (nitrite) and venous blood sample (~4 mL) drawn. Measurements showed NO2 (a biomarker of nitric oxide availability) increased by 138% 2.5 hours after ingestion and resulted in a 6 mm Hg (5%) reduction in systolic blood pressure. No alteration in these parameters was seen with PL ingestion. The researchers attribute the physiological effects observed after BR to be mediated through the systemic reduction of nitrate-derived nitrite to the potent vasodilator and signaling molecule, nitric oxide.

The results indicate that acute dietary nitrate supplementation with BR may lead to a significant and practically meaningful enhancement of performance in cyclists. More investigation on a larger cohort is warranted.

Broccoli targets cancer cells

Sulforaphane (SFN) is an isothiocyanate derived from cruciferous vegetables such as broccoli and broccoli sprouts. Epidemiologic studies suggest that cruciferous vegetable intake may lower the overall risk of cancers including prostate cancer. It is thought that the ability of SFN to inhibit histone deacetylase (HDAC) enzymes may be one mechanism by which it acts as a chemopreventive agent. The aim of this in vitro study was to investigate the protective and therapeutic role of SFN in prostate cancer.

Researchers used normal prostate epithelial cells (PrEC), benign hyperplasia epithelial cells (BPH1), androgen dependent prostate cancer epithelial cells (LnCap), and androgen independent prostate cancer epithelial cells (PC3). Cells were cultured at 5% CO2 and 37°C.

SFN was shown to preferentially induce apoptosis in BPH1 and PC3 cells (P <0.01). Apoptosis was observed following 48 hours of SFN treatment indicated by increases in multiparameter activity. SFN was also shown from caffeine and alcohol 6 and 24 hours before each test respectively.

Following the 4km TT, compared with PL, BR ingestion reduced completion time in all nine participants with a group mean reduction of 2.8% (BR 6.27 ± 0.35 min, P <0.05). Following the 16.1 km TT, relative to PL, BR ingestion reduced completion time in all nine subjects with a group mean reduction of 2.7% (BR 26.9 ± 1.8 min, P <0.01).

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On test days participants had blood pressure measured (four times) and a venous blood sample (~4 mL) drawn. Samples were subsequently analysed for plasma (nitrite) (NO3). Participants then ingested 500 mL of either organic beetroot juice (BR) containing ~6.2 mmoL of NO3 or placebo (PL) organic nitrate depleted BR containing ~0.0047 mmoL of NO3. PL was otherwise similar to the experimental beverage in appearance, odour, taste and texture.

Participants returned to the laboratory on four occasions to complete each of the following assessments:
• 4 km time trial (TT) after nitrate rich BR supplementation
• 4 km TT after nitrate depleted PL supplementation
• 16.1 km TT after BR supplementation
• 16.1 km TT after PL supplementation.

A 48 to 72 hour washout period separated each TT. For the 24 hours preceding the first TT participants recorded their food and fluid intake and physical activity; they were instructed to replicate these in the 24 hours before subsequent TT. Subjects were asked to refrain from caffeine and alcohol 6 and 24 hours before each test respectively.

Following the 4km TT, compared with PL, BR ingestion reduced completion time in all nine participants with a group mean reduction of 2.8% (BR 6.27 ± 0.35 min, P <0.05). Following the 16.1 km TT, relative to PL, BR ingestion reduced completion time in all nine subjects with a group mean reduction of 2.7% (BR 26.9 ± 1.8 min, P <0.01).

Measurements showed NO2 (a biomarker of nitric oxide availability) increased by 138% 2.5 hours after ingestion and resulted in a 6 mm Hg (5%) reduction in systolic blood pressure. No alteration in these parameters was seen with PL ingestion. The researchers attribute the physiological effects observed after BR to be mediated through the systemic reduction of nitrate-derived nitrite to the potent vasodilator and signaling molecule, nitric oxide.

The results indicate that acute dietary nitrate supplementation with BR may lead to a significant and practically meaningful enhancement of performance in cyclists. More investigation on a larger cohort is warranted.

Broccoli targets cancer cells

Sulforaphane (SFN) is an isothiocyanate derived from cruciferous vegetables such as broccoli and broccoli sprouts. Epidemiologic studies suggest that cruciferous vegetable intake may lower the overall risk of cancers including prostate cancer. It is thought that the ability of SFN to inhibit histone deacetylase (HDAC) enzymes may be one mechanism by which it acts as a chemopreventive agent. The aim of this in vitro study was to investigate the protective and therapeutic role of SFN in prostate cancer.

Researchers used normal prostate epithelial cells (PrEC), benign hyperplasia epithelial cells (BPH1), androgen dependent prostate cancer epithelial cells (LnCap), and androgen independent prostate cancer epithelial cells (PC3). Cells were cultured at 5% CO2 and 37°C.

SFN was shown to preferentially induce apoptosis in BPH1 and PC3 cells (P <0.01). Apoptosis was observed following 48 hours of SFN treatment indicated by increases in multiparameter activity. SFN was also shown from caffeine and alcohol 6 and 24 hours before each test respectively.
to selectively reduce several class I and class II HDAC proteins in BPH1, LnCap and PC3 but not normal PrEC prostate cells (P <0.01).

These results indicate that not only is SFN effective at targeting cancer cells through multiple chemopreventative mechanisms, it does not affect (and is therefore safe in) normal tissues.

This study provides further support for the relevance of SFN as a dietary HDAC inhibitor and chemopreventive agent by showing that SFN can selectively target BPH1, LnCap and PC3 prostate cells while leaving normal PrEC prostate cells virtually unaffected.

Breast feeding and child behaviour

In most observational studies breastfed children have had fewer behavioural problems than formula fed children. However these results have been dismissed previously due to too many confounding factors.

Behavioural problems are defined as inappropriate behaviours that occur repeatedly over a period of time, have a negative impact on the child’s development and interfere with the child’s or their family’s everyday life. These may encompass emotional symptoms (e.g. clingy behaviour, anxiety), hyperactivity (e.g. restlessness) or conduct problems (e.g. lying, stealing).

This study examined whether the duration of breast feeding (at all or exclusively) was associated with parent rated measures of behavioural development in children aged 5 years. The Millenium Cohort Study (MCS) is a survey of infants born in the UK during a 12 month period in 2000–2001.

Baseline data was collected by trained interviewers when the cohort infants were 9 months, after which participant households were followed up with home interviews at 2 year intervals. Child behaviour was assessed using a parent completed questionnaire, the Strengths and Difficulties Questionnaire (SDQ).

The analyses included 10,037 mother/child pairs from white ethnic background (9525 term and 512 preterm children). Mother/child pairs from non white and mixed ethnic groups were excluded due to a considerable proportion (36%–41%) of these not responding to the SDQ. Children born extremely prematurely (before 28 weeks of gestation) were excluded because of their complicated feeding patterns during the first months which may not have been adequately captured in the MCS.

Breastfeeding initiation was equally common in term and preterm children (65% in both groups). Twenty-nine per cent of term children and 21% of preterm children were breast fed for at least 4 months (mean duration of breast feeding 9.8 and 9.6 months respectively). A larger proportion of preterm (15.2%) than term children (11.9%) had abnormal total SDQ scores.

The study found that abnormal SDQ scores were less common in breastfed than formula fed children, confirming data from previous studies.

Term children breastfed for 4 months or longer (n = 2741, 29%) had lower odds of an abnormal total SDQ score. After adjustment for potential confounders (socioeconomic factors, mother’s mental health, mother/baby attachment, early childhood exposures), exclusive breast feeding for 4 months or longer was associated with lower odds of abnormal emotional and conduct scores.

The effect of breast feeding on emotional and prosocial subscores in preterm children could not be estimated due to the small numbers of children with abnormal scores. Longer duration of breast feeding was associated with lower odds of abnormal SDQ total and subscores however results were not statistically significant.

The researchers proposed that the association of breast feeding with child behaviour is due to beneficial compounds in breast milk including large amounts of essential long chain polyunsaturated fatty acids (LCPUFAs), growth factors and hormones. These play an important role in the development and function of the brain and central nervous system.

A further factor is that breast feeding leads to more interaction between mother and child, better learning of acceptable behaviour and fewer behavioural problems. However in this analysis having been breast fed for 4 months or longer was associated with fewer behavioural problems independently of mother/baby interaction.

Some limitations to this study include possible recall bias by parents (mothers) interviewed, possible exposure misclassification, inability to assess types of formula/supplemental milks fed to infants and only involving white singleton children.

Probiotic foods protect against preeclampsia

Preeclampsia is a serious condition occurring in pregnancy associated with raised blood pressure (hypertension) and proteinuria. The condition is one of the leading causes of maternal death worldwide and estimated to influence between 2% and 8% of all pregnancies. The etiology and pathogenesis of preeclampsia are not fully understood but increasing evidence suggests an excessive maternal inflammatory response to pregnancy.

The metabolic markers of systemic inflammation, increased in preeclampsia, are closely related to oxidative stress. The gastrointestinal tract represents the largest immune interface with the environment. Probiotics are known to modulate gastrointestinal health through suppression of pathogenic bacteria and to affect human health by pathophysiological processes involved in
The aim of this observational study was to investigate the association between consumption of probiotics in milk-based products and the development of preeclampsia using a large prospective cohort of Norwegian women. The researchers hypothesised that intake of food with probiotics might delay and reduce incidences of preeclampsia in general, particularly early onset or severe preeclampsia, through the reduction of inflammatory responses. Participants were part of the Norwegian Mother and Child Cohort Study (MoBa) involving 33,399 primiparous women over the years 2002–2008.

Participants were asked to provide biologic samples and to answer three questionnaires during pregnancy addressing food, health, exposures, lifestyles and background factors. The intake of milk-based products containing probiotic lactobacilli was estimated from a self-reported food frequency questionnaire.

The MoBa food frequency questionnaire was completed in weeks 17–22 of gestation. The questionnaire asked how often the women had consumed subtypes of milk and yogurt, clearly distinguishing probiotic milk or yogurt from other milk items. Information regarding the use of probiotic supplements was not included in the study. However, in a more recent subsample of the cohort less than 0.5% of the women had reported use of supplements containing probiotic substances.

In Norway all pregnant women receive free antenatal care. Blood pressure measurement and urinalysis for protein are carried out at each antenatal visit; these results were included in the study’s data. The diagnostic criterion for preeclampsia is blood pressure >140/90 mm Hg after 20 weeks’ gestation, combined with proteinuria ≥+1 dipstick on at least 2 occasions.

Preeclampsia is diagnosed as severe preeclampsia if blood pressure is ≥160/110 mm Hg. During analysis researchers considered the following influencing factors: maternal pre-pregnant body mass index, height, educational attainment, smoking status, dietary supplement use and total energy intake.

Among the 33,399 nulliparous women, 1,755 (5.3%) developed preeclampsia. Women with preeclampsia reported lower consumption of probiotic milk products than women without preeclampsia, while the intake of other (non probiotic) milk products did not differ between both groups.

High intake of probiotics (intake of at least 140 mL daily) was associated with reduced risk of all preeclampsia (OR = 0.80, 95% CI: 0.66, 0.96), although the association was most prominent for severe preeclampsia (OR = 0.61, 95% CI: 0.43, 0.89). The incidence of preeclampsia was 5.6% among participants not consuming probiotics and 4.1% among high consumers. The incidence of severe preeclampsia was 1.8% among non-consumers of probiotics and 1.0% in the high intake group.

The energy-adjusted intakes of protein and dietary fibre were lower in participants who developed preeclampsia than in those who did not. The prevalence of severe preeclampsia was 2.5% in overweight and 1.2% in normal weight women. The protective effect of any probiotic intake was evident in both groups but was stronger in normal weight women (OR = 0.74, 95% CI: 0.58, 0.95) than in overweight women (OR = 0.83, 95% CI: 0.62, 1.10).

This large observational study indicates an independent protective association between intake of probiotic milk products and preeclampsia, especially severe preeclampsia. More research is warranted to assess dose and duration of probiotic supplementation in the treatment and prevention of preeclampsia.

**Sugar sweetened beverages and BP**


Established modifiable risk factors for elevated blood pressure (BP) are high sodium intake, inadequate potassium intake, high body mass index (BMI) and excessive alcohol intake. Other dietary factors possibly related to adverse BP levels include low intakes of calcium, magnesium, phosphorus, iron, vegetable protein, glutamic acid, polyunsaturated fatty acids and starch; and high intakes of cholesterol, animal protein and red meat.

This cross-sectional population study assessed the role of sugar sweetened beverages (SSBs) in the development of elevated BP. Researchers examined association with BP and SSBs, diet (noncaloric sweetened) beverages, and sugars (fructose, glucose and sucrose) for 2,696 participants of the International Study of Macro/Micronutrients and Blood Pressure (INTERMAP) from 10 population samples in the United States and the United Kingdom.

Participants were randomly recruited from general and occupational populations. Each participant was evaluated 4 times, the first two visits on consecutive days, the second two visits on consecutive days an average of 3 weeks later. BP was measured twice at each visit. Measurements of height and weight and questionnaire data on daily alcohol consumption over the previous 7 days were obtained at two visits. Dietary data was collected at each visit.

Each participant provided two 24-hour urine collections, start and end timed at the research center; measurements included urinary volume and sodium, potassium, calcium, magnesium, urea and creatinine levels. Urinary sodium, potassium and urea excretion were used to validate dietary intake of sodium, potassium and protein.

Sugar sweetened and diet beverage intakes were estimated from food records. SSBs included non...
carbonated and carbonated soft drinks, fruit drinks (excluding 100% fruit juices) and lemonade, excluding diet beverages.

Measurements per person were averaged across the 4 visits for beverage, nutrient and BP variables and across the two collections for 24-hour urinary variables.

Mean SSB and diet beverage intakes were higher in the United States than the United Kingdom with a mean SSB intake of 0.9 servings per day (306 mL/24 hours) in the United States and 0.2 servings per day (66 mL/24 hours) in the United Kingdom.

Compared with participants who consumed no SSBs adjusted mean energy intake was higher by 120 kcal/24 hours for those who consumed ≤1 serving per day (≤355 mL/24 hours) and was higher by 397 kcal/24 hours for those who consumed ≤1 serving per day. SSB intake higher by 1 serving per day was associated with a systolic BP difference of +1.6 mm Hg (z=4.98; P<0.001) and +1.1 mm Hg (z=3.40; P<0.001) with control for weight and height. Higher intake of SSBs was associated with more adverse overall nutritional quality.

These findings show a direct association between SSB consumption and BP and direct associations of fructose and glucose intake with BP that were stronger among individuals with higher urinary sodium excretion. This has been attributed to the effect of SSB/fructose on the uric acid pathway.

Fructose consumption may lead to increased serum uric acid via phosphorylation of fructose by hepatocytes and generation of adenosine diphosphate which is metabolised to uric acid. Raised serum uric acid may influence BP by reducing levels of NO, a potent vasodilator. Sugar consumption has also been linked with enhanced sympathetic nervous system activity and sodium retention.

These results support health recommendations to reduce or eliminate intake of SSBs and sugars particularly in individuals predisposed to elevated BP and cardiovascular disease.

**Zinc supplementation reduces the duration of a common cold**


This systematic review aimed to examine the relationship between the total daily dose of zinc (from lozenges) and its effect on the duration of colds in patients with natural common cold infections. The Medline, Scopus and Cochrane Central Register of Controlled Trials data bases were searched for placebo controlled trials examining the effect of zinc lozenges on the duration of a common cold.

The review was restricted to trials examining the therapeutic effect of zinc lozenges on natural common cold infections. As an inclusion criterion a concurrent placebo group was required as clinically relevant common cold outcomes are largely subjective and explicitly different interventions (i.e. no placebo in one arm) might bias the comparison. Studies with adults and children were both included.

Thirteen double blind placebo controlled comparisons have examined the therapeutic effect of zinc lozenges on the duration of common cold episodes of natural origin. The total number of common cold episodes in these trials was 1407.

None of the five comparisons that used less than 75 mg/day of zinc found an effect of zinc lozenges whereas seven of the eight comparisons which used over 75 mg/day of zinc found a statistically significant benefit. In the eight high dose trials the zinc lozenges reduced the duration of colds by 32% (95% CI: 27% to 37%). All studies showed there was a significant difference between zinc and placebo.

In several trials the zinc lozenges caused acute adverse effects such as bad taste and constipation but none of the trials reported long term harm.

Even though the same dose of zinc could be used in two different lozenges, other constituents may lead to substantial differences in the levels of free zinc ions and therefore bioavailability. Four trials used 80 to 92 mg/day and observed significant benefit. Three of these used lozenges containing zinc acetate which does not form complexes with zinc ions.

Pooling the three high dose (>75 mg/day) zinc acetate trials gives a mean effect of 42% reduction in the duration of colds. Five high dose (>75 mg/day) trials used zinc salts other than acetate. Pooling these results gave a mean effect of 20% (95% CI: 12% to 28%) reduction in the duration of colds.

This data highlights the role of zinc in acute management of the common cold notably at doses above 75 mg/day and complexed with acetate.
Weighing in at nearly 1600 pages *Clinical Naturopathic Medicine* makes a substantial contribution to the genre of contemporary CAM texts that integrate holistic traditional approaches with evidence based practice. Well known naturopath Dr Joseph Pizzorno describes this book as an outstanding one that “will have a profound impact on improving the clinical quality and efficacy of our profession”. Does it live up to this high praise?

Lead author, Leah Hechtman, is Vice President of the National Herbalists Association of Australia as well as a university lecturer and experienced naturopath. She has assembled an impressive team of experienced practitioners and academics to collaborate on this comprehensive text.

The structure of the book is logical and easy to follow. It is divided into 5 parts and focuses on the key naturopathic treatments of nutritional medicine, herbal medicine and lifestyle recommendations.

Part 1, Principles of Naturopathic Medicine, consists of 4 chapters covering the philosophy of naturopathy, the principles of nutritional medicine, the principles of herbal medicine and an introduction to herb/nutrient drug interactions. Included in this section is a description of the historical highlights that have shaped the profession. There is also an interesting review of the current position of naturopathy within the Australian healthcare system.

Part 2, Naturopathic Treatments, provides an overview of the key practices of nutritional medicine and herbal medicine. Whilst the nutritional medicine chapter briefly mentions food and diet the focus is on supplementation. Perhaps a section on fresh juices and phytochemicals could be squeezed into the next edition? The chapter on herbal medicine provides useful lists of herbs relevant to each body system and grouped according to their pharmacological actions. For example listed under the heading of ‘gastrointestinal system’ are antacids, anthelmintics, antiemetics, carminatives, demulcents, gastrointestinal anti-inflammatories, gastrointestinal astringents, gastrointestinal spasmyloytics, laxatives and mucous membrane trophorestoratives.

The next 12 chapters make up Part 3 of the book, Body Systems. Each system of the body, together with relevant conditions and treatments, is comprehensively covered incorporating both traditional naturopathic practices and scientific evidence. These chapters are densely packed with useful information and case studies. However the presentation of the scientific evidence could be much improved by including a grading system such as that recommended by the NHMRC.

Fertility, pregnancy, breastfeeding and pediatrics are covered in part 4, The Lifecycle. The chapter on pediatrics includes some controversial statements such as the suggestion that ‘liver is the most suitable source of arachidonic acid’ for infants who are 100% formula fed. Those with a passion for evidence based practice might feel agitated by some of the advice in this important chapter.

Part 5 consists of 8 appendices for miscellaneous tables including a herbal medicine dosage chart and a list of herbs that are contraindicated during pregnancy and lactation.

Whilst some chapters contain helpful diagrams and photos the overall ratio of words to visual aids in this book favours those readers who can handle long stretches of narrative without any scenery.

This comprehensive text will be a valuable resource for students of naturopathy, nutritional medicine and herbal medicine. Experienced naturopaths and integrative medical and allied health professionals will find many sections useful but this is a hefty book for the shelves rather than a concise clinical desktop reference.

The book has a scratch off panel concealing a PIN on the inside cover to allow purchasers access to the complete contents of the book online.

Available for non postal loan from the NHAA Library.
Medicinal Plants in Australia
Volume 2 Gums, Resins, Tannin and Essential Oils
By Cheryll Williams
Rosenberg Publishing Dural Australia 2011
ISBN 978 1 877 05894 3
Reviewed by Bettina Schmoll

This is the 2nd in a series of four by Cheryll Williams and her passion for Australian natives is obvious. The introduction links the research of today with the history of yesterday and her thoughts on our poor care of our native landscape is already made clear. I’m not sure why she has included 1½ pages on orchids in the introduction of a book titled *Gums, Resins, Tannin and Essential oils*, however the photos are lovely.

The historical information is wonderfully integrated throughout the book and anyone wanting to connect more with our past would find this book a must. This combines smoothly with supportive current information. For example in chapter 1, *Oleum eucalypti*, the focus is on Eucalyptus with beautiful photos including a colour plate from 1790 and the more recent references covering the chemical constituents of the essential oils, an excellent addition not only in this but also in other chapters.

Utilisation of drawings, lithographs and photos with use of botanical names is an absolute delight for a herbalist and teacher of basic botany such as myself. I cannot imagine how long it took to compile the tables of essential oil constituents throughout the book. Table 1.1 for example, the summary of the main chemical constituents found in *Eucalyptus* species, is 7 pages of fully referenced information.

Chapter 2 is devoted to kino, the resinous exudate from the gums. The author combines traditional information well with the contemporary and provides a table referring to plants which are a source of kino. This is expanded upon in chapter 3, Resinous Resources, and also discusses the concern with coumarin containing plants.

Chapter 4 on native pines provides valuable information for the botany student on gymnosperms, including *Ginkgo biloba* with great photographs.

Despite the fact that chapter 5 is titled The Myrtaceae: Hidden Chemical Treasures, I was disappointed to find no mention of the *Backhousia* spp. Lemon myrtle (*Backhousia citriodora*) has become the second biggest native crop in Australia and some of its exceptional medicinal benefits were published in September 2009 in a RIRDC report. Why include information and a photo of lemongrass (*Cymbopogon* spp), which is not in the Myrtaceae family and is not native to Australia?

The chapter on tannins and trees focuses on the *Acacia* family, wattles and eucalypts. Tannin categories are presented in tabular format, very comprehensive and the chapter expands on plants high in anthocyanidins. Focus is on bilberries and raspberries with unfortunately no mention of Tasmanian pepper leaf, Davidson’s plum or riberry whose anthocyanidin content is worth mentioning.

The wattle and *Acacia* genera and their value in revegetation as well as those which are considered weeds is covered in chapter 7. Chapter 8 then focuses on their medicinal uses and the author provides a comprehensive table with the common names, uses, treatment details (which include indigenous use) and the reference sources.

Research into tea tree essential oil is covered well in chapter 9 and even aromatherapy students will benefit greatly from the information throughout this chapter. The essential oil components of *Baeckea*, *Kunzea* and *Leptospermum* genera (the author calls them species) is extremely well represented in table form.

The last chapter is called Melaleuca: The Prosaic Paperbark, but also discusses orchids. There are 4 tables in this chapter which even address oils known for their 1,8 cineole content as well as those with a commercial or medicinal potential. Again excellent information.

The book reviews are available in the NHAA library reference only.
AJMH based CPE Questionaire

The AJMH based CPE questionnaire system is a voluntary system designed to assist members in the accumulation of NHAA CPE points. Questions are divided into the appropriate subject categories (herbal medicine and medical science) and each question refers to an article in this issue of the Australian Journal of Medical Herbalism. Points accumulated through completion of these questions should be recorded in the NHAA CPE diary. Each completed question is worth one mark in the relevant category. Your completed CPE diary should be returned with your membership renewal at the end of the financial year. For further information please see the NHAA CPE Member's Manual on the NHAA website www.nhaa.org.au.

Herbal medicine questions - AJMH 23(3)

According to each article which statement is most correct?

1. **Bacopa for memory and learning**
   a) *Bacopa* given for 16 weeks improved cognitive function but had minor side effects.
   b) *Bacopa* given for 16 weeks improved cognitive function but had no effect on working memory.
   c) *Bacopa* given for 16 weeks improved verbal span tests and cognitive function but had side effects.
   d) *Bacopa* given for 16 weeks improved verbal span tests and cognitive function and was well tolerated.
   e) Improvements in cognitive function and memory were similar in both the *Bacopa* and placebo groups.

2. **Medicinal plants for dermatological disorders**
   a) *Solanum nigrum* is used for treatment of goiter.
   b) *Solanum* and *Juglans* species are traditionally used for treatment of frost bite.
   c) *Azadiracta indica* is traditionally considered an effective treatment for topical fungal infections.
   d) Only a) and b)
   e) All of the above.

3. **Herbal medicine for Helicobacter pylori**
   a) Cranberry juice has been shown to have an anti-adhesion effect on *Helicobacter pylori* bacterium adhesion in the gut.
   b) Drinking 250 mL cranberry juice twice daily is only effective in treating *H. pylori* if used for more than 90 days.
   c) Garlic oil is most effective for treatment of *H. pylori* when used in an alkaline stomach environment.
   d) Only a) and b)
   e) All of the above.

4. **Reduce skin ageing with gotu kola?**
   a) *Centella asiatica* as a cream has no effect on cellulite.
   b) Irbic acid from *C. asiatica* inhibits macrophage activity.
   c) Irbic acid from *C. asiatica* may increase collagenase activity.
   d) Irbic acid from *C. asiatica* could be a useful in reducing skin ageing.
   e) *C. asiatica* may provide new compounds for natural sunscreens.

5. **Herbal treatment of rheumatoid arthritis**
   a) Lei gong teng is more useful in osteoarthritis than rheumatoid arthritis.
   b) TwHF extract proved more clinically useful in RA than sulfasalazine.
   c) TwHF extract affected radiological progression of RA but not symptoms of the disease.
   d) There were no adverse effects in participants taking the herbal medicine.
   e) This study was not deemed worthy of being reported in conventional medical literature.

Medical science questions - AJMH 23(3)

1. **Monitoring cancer patients**
   a) Gene therapy is reducing the incidence of cancer worldwide.
   b) The use of CAM therapies increases the feeling of wellbeing and hope in cancer patients.
   c) Mammograms have no cumulative radiation effect.
   d) PET scans are most effective in detecting early stage tumours.
   e) Infectious agents such as *Helicobacter pylori*, hepatitis B and C, Epstein-Barr virus or human papillomavirus do not appear to be implicated in the development of cancer.

2. **Helicobacter pylori**
   a) There is currently no link between *H. pylori* infection and the gastric carcinomas.
   b) *H. pylori* infection can only be caught through person to person transmission.
   c) *H. pylori* infection is a precursor to chronic gastritis, peptic and duodenal ulceration.
   d) *H. pylori* is destroyed by the acid environment of the stomach.
   e) All of the above.

3. **Zinc supplementation**
   Zinc supplementation was shown to be effective in the common cold at what dose:
   a) 15-30 mg daily
   b) 30-60 mg daily
   c) 75 mg daily
   d) Over 75 mg daily
The NHAA invites contributions to the Australian Journal of Medical Herbalism.

The Australian Journal of Medical Herbalism publishes material on all aspects of medical herbalism with emphasis on the philosophy of medical herbalism and the phytochemistry, pharmacology and clinical applications of medicinal plants.

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• All statements must be referenced and a full reference list must be included. If the statement is the author’s observation or opinion this should be made clear.
• All statements should be of a professional nature and exclude any inflammatory, derogatory, racist or other inappropriate style of writing.
• Papers should be no more than 5000 words including tables and references. The number of references should not exceed 30 (except for review articles).
• An abstract of the article should be included.
• A brief profile of the author should be included.

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Text citation should appear as surname of first author and year of publication in parentheses at the end of a statement or paragraph such as (Cowper 2007).

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