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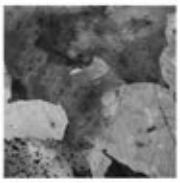

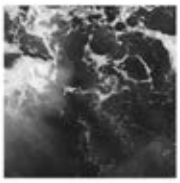

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Editorial

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Welcome to the last edition of 2013. I have thoroughly enjoyed my first year as Editor and thank you for the support and feedback I have received since embarking on this role. The Editorial Board and I have learnt an enormous amount about the journal's readership during this time and as a result have endeavoured to publish clinically relevant research and review articles, together with topical commentary and discussion pieces. I have no doubt that the journal will continue to evolve throughout 2014 and beyond.

It was evident from the NHAA member surveys conducted earlier in the year that many practitioners would like to learn more about writing for publication. In response to this we delivered a workshop in Sydney entitled 'Writing for Publication' which provided a general overview of preparing a manuscript, with particular focus on writing case studies. It was clear from the feedback prior to the event that many members from outside the Sydney area would also like to attend similar workshops and we are investigating ways to do this. In the meantime, please continue to provide input on how we can continue to make the journal worthwhile and relevant.

I would like to extend a very wholehearted thank you to all the reviewers who have contributed their expertise to the journal in 2013. The strength of the journal lies with the reviewers who give their time and skill to improve the quality of our publication. Thank you to Dr Abigail Omolayo Aiyepola, Ms Diana Bowman, Mr Ian Breakspear, Mr David Casteleijn, Mr Greg Connolly, Mr Rik Danenberg, Dr Michael Evans, Dr Stuart Glastonbury, Ms Assunta Hunter, Ms Catherine Johnson, Ms Lisa Marasco, Dr Mradu Gupta, Dr Paulo Moraes, Ms Annette Morgan, Ms Helen Padarin, Ms Anita Pierantozzi, Dr Sokcheon Pak, Ms Jeannie Radcliffe, Mr Jason Rainforest, Mr Rob Santich, Dr Jerome Sarris, Ms Janet Schloss, Dr Madhu Sharma, Dr Joshua Smith, Mr Michael Thompson, Dr Graeme William Tobyn, Dr Kyril Turpaev, Mr Mark Webb, Mr Greg Whitten, Dr Jenny Wilkinson and Dr Hans Wohlmuth.

I would also like to extend my personal gratitude to the Associate Editors who contribute significantly to the quality of the journal: Dr Andrew Pengelly, Dr Amie Steel, Dr Janelle Wheat, Ms Dawn Whitten and Dr Hans Wohlmuth.

The current issue contains two articles with a historical focus. The first by Justin Sinclair, entitled 'The alchemy of herbal medicine: spagyric tinctures, elixirs and the vegetable stone', discusses the evolution and history of spagyrics and details the principle steps in manufacturing the spagyric tinctures, elixirs and *Lapis vegetablis* (vegetable stone). Phillipus Aureolus Theophrastus von Hohenheim (Paracelsus, 1493-1541CE), often considered a father of modern toxicology, was the first to write extensively on the subject of spagyrics. The second article is by Karen McElroy and is entitled 'Anthroposophic medicine: deepening our understanding of herbs, healing and the human being'. Anthroposophic medicine is a philosophy and system of medicine that hails from Europe and was founded by the Austrian scientist and philosopher, Rudolf Steiner (1861-1925). Steiner's studies varied widely and included the natural sciences, botany, chemistry and physics. He was also significantly influenced by the German philosopher, politician, writer and naturalist, Johann Wolfgang von Goethe (1749-1832). Steiner devised a framework for understanding the universe and our distinct interconnectedness to all things. This system of medicine aims to collate ancient medical knowledge with contemporary scientific research.

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To the Editor

Dear Editor,

Thank you for publishing the two articles by Dr John Wardle in last month's edition of the Australian Journal of Herbal Medicine. The article 'Independent registration for naturopaths and herbalists in Australia: the coming of age of an ancient profession,' was timely and provides a comprehensive overview of the past and current situations. The primary goal of registration is to safeguard the public; however, it does bring benchmark standards to our profession, particularly in relation to education and practice. It brings a known place within the general health care system by removing us from the 'unregistered practitioners' category. It is apparent that naturopathic colleges tend to provide vocationally based qualifications compared to university Bachelor degrees, which also aim to develop critical thinking skills. It was interesting to read how private colleges protected their own financial interests by investing in a fighting fund to resist the development of a degree education for naturopaths and Western herbalists. I wonder how the educational background of members has influenced the collective consciousness of our profession, particularly if most members have obtained their qualifications from private colleges. Critical thinking is an important skill for effective debate.

Like many of your members, I obtained my primary qualification to practice through a private college back when universities did not offer the Bachelor of Naturopathy. It was in my fourth year (full-time) that Southern Cross University started their Bachelor course, and a few teachers made the move to Lismore to take up lecturing positions. The message from the college was that private education remained better for the 'naturopathic' subjects, as it was less likely to be subjected to mainstream 'scientific' ideology. In other words, a college education had a progressive character that was particularly beneficial for those who wanted to practice 'alternative medicine' i.e. outside the mainstream philosophical medical paradigm (for want of a better word) using alternative scientific epistemology.

It is interesting to reflect upon changes in other disciplines at the time. Medical schools were thinking along the same 'alternative' lines with their introduction of patient-centred teaching and problem-solving approaches incorporated into the education of doctors. Education in health disciplines such as nursing, midwifery and women's health embraced new patient-centred models of care where the needs of patients (or clients) were identified and addressed in an individual way, incorporating health promotion and prevention of disease as well as treatment. Indeed, it was not long before the establishment of the naturopathic degree at Southern Cross University that nursing education moved away from the hospital system (vocationally-based education) and into the university system, perhaps with the goal of fostering critical thinking skills among nurses. Even legal disciplines adopted alternatives with the introduction of alternative dispute resolution and a tiered, user-focused system.

So, is the private college education of naturopathic subjects actually better than that of a university? It is possible that presenting the college-based education as superior is mainly furthering the vested interests of private college owners rather than actually providing excellent education for naturopaths and Western herbalists. What is the impact on the profession considering that the education of many members was and is vocationally based and critical thinking skills are not developed or valued? It is ironic to think that our profession may largely contain practitioners that use a mechanistic vocational approach, that follow instructions and rules in much the same way an apprentice builder learns how to build a house or a hairdresser learns how to colour hair, while only those exposed to a university education may have learned how to interpret, analyse and evaluate the ideas and arguments behind the process – in our case, our practice.

A measure of our profession's capacity for critical thinking could be gauged by our response to the proposed recent changes presented by the Therapeutic Goods Administration (TGA) regarding the advertisement of practitioner-only products. The main concern voiced by the profession was that we will be deprived of a source of information. However, that particular concern distracts from an underlying bigger issue which reflects our limited capacity for critical thinking; that is, our reliance on promotional material from supplement manufacturers for information or instructions. Although the promotion of supplements may occur in an educational context, it is, at its heart, promotion of business and sales of supplements. Private college education is provided with much the same goals. The entire purpose of the process is to attract and retain students, and to increase income and profits for proprietors. Like you, I have attended many company seminars and gained 'valuable clinical insights.' However, it is a fine line between sources of objective information informing practice and persuasive statements designed to make you feel as though the product, item or agenda is essential and you need to buy more.

The question begs for those of us with a private college education: have we developed adequate critical thinking skills in order to debate and navigate our own way, to face our challenges, build our identity as a

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Primum non nocere. Are we really keeping our patients safe? Interprofessional communication between CAM and medical practitioners

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Teamwork and communication failures are the leading cause of patient safety incidents in health care (Canadian Patient Safety Institute 2011)

Use of complementary and alternative medicine (CAM) in Australia is considerable (MacLennan 2006, McCabe 2005, Xue 2007), with more than two-thirds of the adult population using at least one form of CAM, and 44% reporting visiting a CAM practitioner in the previous 12 months (Xue 2007). The growth of CAM has raised many issues within the literature, the most common relating to safety, efficacy and regulation of CAM (MacLennan 2006, Shorofi and Arbon 2010, Robinson and McGrail 2004, Goldman 2008, Wardle 2012, Pinto 2008, Spinks and Hollingsworth 2012). However, despite this, the Australian public have continued to seek CAM as a component of their health care, spending in excess of $4 billion annually (Xue 2007).

Parallel to the rise in CAM popularity, Australian medical practitioners are faced with a greater proportion of patients who present using conventional and CAM concurrently (MacLennan 2006, Xue 2007, Shorofi and Arbon 2010). In addition to the documented risks that concomitant use of CAM and conventional medicines pose to patient safety (Davis 2012, Goldman 2008, Mehta 2008, Shalansky 2007), this is further compounded by a large and increasing body of evidence that indicates that non-disclosure of CAM use by Australian patients is relatively high (Shorofi and Arbon 2010, Thomson 2012, MacLennan 2006). In hospital settings, non-disclosure of CAM use escalates patient safety risks due to known interactions between certain CAM therapies and anaesthetic drugs, as well as other pharmaceuticals (Hori 2008, Werneke 2004, Wang 2003). Surgical patients pose considerable risk due to the possibility of haemorrhage (Norred 2002a, Norred 2002b, Norred 2000), a risk further compounded by new oral anticoagulants (e.g. dibigatran and rivaroxaban) now being utilised in Australian hospitals, whose risk profiles are yet to be fully understood (Weightman and Gibbs 2012).

Due to the rapid growth in CAM and its potential to interact with mainstream medicine, emphasis has been placed on medical educators to ensure that medical practitioners have adequate knowledge to effectively and safely manage patients who utilise CAM. The published position statement of the Australian Medical Association (AMA) further endorses this need, indicating that "*medical practitioners should have access to education about CAM in their undergraduate, vocational and further education to provide advice to patients"* (Australian Medical Association 2012). Medical practitioners also support the need for appropriate education on CAM (Cohen 2005); however, the current state of CAM education in Australia is poorly developed, having no formalised requirement for medical schools to include it as a standardised component of the medical curricula. As medical practitioners progress through the prevocational (postgraduate PGY 1-3+) and vocational (specialist) stages of their training, CAM education is also variable. Thus, the onus for acquiring knowledge regarding CAM rests on the individual (Pierantozzi 2013).

As a Medical Education Officer (MEO) working in a metropolitan South East Queensland hospital, I have witnessed deficiencies in many junior doctors' knowledge of CAM and application thereof in patient care, and have subsequently been active in implementing ongoing education sessions for medical students, junior doctors and general practice (GP) registrars across various health services. During these education sessions, doctors indicated through both formal (Pierantozzi 2013) and informal feedback that routine CAM inquiry was infrequent and, for some, dependent on the patient. Subsequently, educating medical physicians about the importance of clinical inquiry into CAM as a standardised component of the history taking and documentation process has been a key theme integrated into the learning objectives of this training package.

However, a recurrent issue identified within these sessions by participants has been interprofessional communication and the lack thereof. GP registrars indicated that the only communication that they received from CAM practitioners was via the patient themselves who presented with a list of investigations "requested by the naturopath" without any explanation. As one GP registrar describes:

"When a patient presents with a list of tests requested by the naturopath without any explanation as to why they are even needed, this just leaves a sour taste in my mouth. If I have to converse with another treating physician

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the least I do is write a referral letter. It's an integral component in the continuity of the patients' care."

Therefore, in addition to the emphasis placed on appropriate CAM education for medical physicians, should we also be considering the importance of interprofessional communication?

It is well documented that communication among health professionals is a highly complex but important function in the provision of safe health care, not only for effective interactions between individuals and their health care providers, but also between the health care providers themselves (Schwartz 2010). Communication breakdowns and teamwork failures have been recognised as key contributing factors in the occurrence of patient safety incidents, and were the primary root cause in more than 70% of sentinel events (Leonard 2004). As the Australian public continue to use CAM, communication between CAM and medical practitioners should be emphasised, particularly as the potential for interactions and subsequent patient safety events is increased. As one GP registrar notes:

"The communication between doctors and CAM practitioners is even more important when patients are using herbal medicines and pharmaceuticals together because we need to ensure that the patient is safe and their management plan is not impacted by interactions. I support patients' use of CAM but when I don't know what they are using and I have no communication with the herbal practitioner it's hard to provide safe and effective treatment"

Although the majority of doctors involved in the CAM education sessions, particularly GP registrars, indicated a positive attitude towards interprofessional communication, informal group discussions thus far reveals that most rarely initiate communication with CAM practitioners. This is consistent with published literature which indicates that although GPs have a positive attitude towards interprofessional communication, low rates are recorded in practice (Ben-Arye 2007). Similar results have been observed across other health care disciplines including midwifery, where a recent Australian study found that despite 83% of midwives supporting the existence of formal communication, less than one quarter (22%) initiated formal communication with CAM practitioners (Diezel 2013). Equally, CAM practitioners also share responsibility to enquire about their patients' conventional care, with survey data indicating that only a small percentage of CAM providers will initiate communication with their patients' physicians (Sherman 2005, Ben-Arye 2007, Schiff 2011). Consequently, a low patient-disclosure rate of CAM use, coupled with poor physician-CAM provider communication, combine to create a "Bermuda Triangle" phenomenon where valuable information disappears (Schiff 2011).

Efforts to improve teamwork and communication between the disciplines must build upon shared values and practice methods that support the creation of a patient safety culture; however, this may not necessitate the 'reinvention of the wheel'. Although a number of initiatives for improving communication between the disciplines have been described in various settings (Nedrow 2007), including suggestions of an appropriate mode and content of communication (Schiff 2011), as an MEO working with medical practitioners on a daily basis, the ability to speak 'the same structured language' has been a vital skill that I have learnt and utilised in both written and verbal communications. Language barriers caused by distinct health philosophies and associated terminology tend to complicate communication (Soklaridis 2009, Allareddy 2007); however, standardised tools and behaviours from the aviation industry, such as Situation-Background-Assessment-Recommendation (SBAR), can greatly enhance safety by helping to set expectations for what is communicated and how communication is handled (Leonard 2004).

Originally introduced within the health care domain to help structure communication between nurses and physicians in acute settings (Leonard 2004), with positive results including improvement in staff and patient satisfaction, clinical outcomes, team communication, and patient safety culture (Leonard 2004), the SBAR technique has now been implemented within interprofessional teams (Leonard 2004, McFerran 2005, Uhlig 2002). A recent study found that SBAR use in an interprofessional rehabilitation setting enabled participants to communicate their concerns in a professional, objective manner with appropriate justification so that their recommendations were heard and adopted (Boaro 2010). In Australia, emphasis has been placed on health service organisations to implement sustainable, systematic processes for effective communication techniques to support safe patient care. This is driven in part by the National Safety and Quality Health Service Standards (NSQHS) published by the Australian Commission on Safety and Quality in Health Care (ACSQHC), which includes a standard specifically relating to clinical handover which describes the systems and strategies for effective clinical communication whenever accountability and responsibility for a patient's care is transferred (Australian Commission on Safety and Quality in Health Care 2011). Subsequently, many Australian health care organisations have implemented standardised communication methodologies, including the SBAR technique or variations of this tool e.g. ISBAR, ISOBAR. This 'standardised structured language' has been identified as such an important skill for Queensland Health staff to acquire that Metro South Hospital and Health Service have mandated Communication and Patient Safety (CaPS) training, including education and application of the SBAR technique, for all clinical and non-clinical staff with great success (Lee 2012). In fact, it was in attending this training that I acquired the SBAR

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Table 1: SBAR (Adapted from (Safer Healthcare 2009, Monroe 2006))

S
Describe the SITUATION
	• Introduce yourself
	• Identify the patient and the reason for your call
	• Describe your concern
	  • The situation I am concerned about is …….
	  • I wish to inform you of ……(e.g. current treatment/s, management plan and possible treatment interactions, changes to patient status, referral to assume the care of the patient for a problem)

B
Provide BACKGROUND
	• What is the relevant supporting background information
	  • Chief complaint/presenting symptoms
	  • *Current status*
	  • *Relevant history, examination and/or test results*
	  • Current treatments and/or management plan

A
Provide client ASSESSMENT
	• State what you think is going on
	  • The problem seems to be……
	  • I am not sure what the problem is, but the client/patient is deteriorating

R **Make RECOMMENDATION**	• What should be done? • What is your recommendation?

skills and knowledge to speak 'the same structured language'.

So what exactly is SBAR and how could this communication technique be utilised to improve interprofessional communication between CAM and other health care professionals? An overview of SBAR and the various elements is provided in Table 1. Development of a common language between CAM and medical practitioners has been shown to be a crucial first step in overcoming the communication gap (Frenkel 2007). Although the use of SBAR is not the only solution to improving interprofessional communication, it may allow CAM practitioners confidence to communicate in a professional and objective manner.

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Training the next generation: advanced diplomas or degrees?

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Abstract: For a little over 10 years the minimum qualification for entry to the profession of naturopathy and Western herbal medicine in Australia has been the Advanced Diploma, as described in the Australian Health Training Package. This commentary piece is drawn from a presentation given at the 8th International Conference of Herbal Medicine. It seeks to profile the current educational context in herbal medicine and naturopathy and examine whether or not the Advanced Diploma is an appropriate qualification level. The author's opinion on the future direction of herbal and naturopathic education is presented with justification.

Naturopathic and Western herbal medicine education in Australia has changed considerably over the last 70 years, moving from informal apprenticeship training to nationally recognised advanced diploma level qualifications and, more recently, a handful of bachelor degree programmes. Yet the desired outcome remains largely the same – to produce effective and safe practitioners of herbal medicine and naturopathy who can work in collaboration with other health professionals within the wider healthcare system.

Jean Piaget (1896-1980), a Swiss development psychologist and philosopher, as quoted in 1988 in "Education for Democracy", Proceedings from the Cambridge School Conference on Progressive Education, stated …

"The principle goal of education in the schools is to create men and women who are capable of doing new things, not simply repeating what other generations have done; men and women who are creative, inventive, and discoverers, who can be critical and verify, and not accept everything they are offered" (Jervis and Tobier 1988).

The question is not whether this goal is relevant to herbal and naturopathic education – the real question is "does our current educational system achieve this goal?" In order to answer this question, we need to understand the current state of naturopathic and Western herbal medicine education in Australia.

Setting the scene

Whilst private educational providers have existed for decades, the 1990's brought a period of significant change in the educational landscape across Australia. Private providers – including those offering naturopathy and herbal medicine training – were seeking parity with public institutions. In particular, they desired the same financial assistance which was being provided to students of public institutions; however, this required far more regulation than had previously existed. Private educational institutions now needed to become Registered Training Organisations (RTO's), meet numerous accountability requirements, and deliver qualifications which fit into one of the National Training Packages.

2002 – The advanced diploma becomes the minimum standard

On December 11 2001, the Australian National Training Authority released the Australian Health Training Package (HTP). The HTP laid out a set of qualification standards for a range of disciplines including (but not limited to) the complementary medicine disciplines. In total, 74 different qualifications were described in this first version of the HTP, ranging from Certificate II to Advanced Diploma (training.gov.au).

The Health Training Package specified only one level of qualification for the disciplines of naturopathy and Western herbal medicine:

- Advanced Diploma of Naturopathy
- Advanced Diploma of Western Herbal Medicine

With the acceptance of the HTP, private colleges changed their course titles and content to fit into these Advanced Diploma specifications. Since its introduction and application in 2002, the HTP has undergone numerous revisions and the national bodies overseeing education standards have changed name and scope. Nevertheless, at the time of writing this article, advanced diplomas remain the minimum nationally recognised qualification for the clinical disciplines of naturopathy and herbal medicine as accepted by professional associations.

What about bachelor degrees?

Since the late 1990's, private colleges have formed articulation arrangements with certain universities so that graduates of their courses can upgrade to bachelor level qualifications. Indeed, RTO's delivering advanced diplomas are now required to demonstrate such an articulation pathway. Whilst the option is available, only some advanced diploma graduates choose to upgrade at this stage and it is not a requirement of entry to the profession. In addition, the number of universities offering this pathway is decreasing as shown by a

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statement on the University of New England website observed in April 2013 which read "Please note that the undergraduate course Bachelor of Health Science and Bachelor of Applied Health are no longer offered at UNE" (University of New England n.d).

Additionally, some private providers have received recognition as higher education (HE) providers and have developed accredited bachelor qualifications in naturopathy and/or Western herbal medicine which they deliver in-house. Whilst these are separate to established university degrees, they meet similar standards and accountability requirements.

Finally, a handful of bachelor level clinical qualifications in naturopathy and/or herbal medicine have been offered at certain universities, including Southern Cross University, University of Newcastle and the University of Western Sydney. However, over the years these courses have been subject to a number of internal and external pressures and, at the time of writing, none of these clinical courses remain open for new students.

What defines advanced diplomas or degrees?

The description of different qualification levels starts with the Australian Qualifications Framework. "The Australian Qualifications Framework (AQF) is the national policy for regulated qualifications in Australian education and training. It incorporates the qualifications from each education and training sector into a single comprehensive national qualifications framework." (Australian Qualifications Framework 2013)

The AQF does not discuss specific disciplines, but rather outlines the standards for the different levels of Australian qualifications. Each level, ranging from 1 to 10, defines the relative depth and complexity, and the expected autonomy of the graduate. The levels and their respective qualifications are best shown in an illustration directly from the AQF.

Advanced diplomas and degrees – the key differences

Whilst a full analysis of the AQF document is very enlightening, it is beyond the scope of this article. For those interested in reading the detail, the AQF, particularly pages 13, 15 and 16, can be reviewed. The document is available freely at http://www.aqf.edu.au/wp-content/uploads/2013/05/AQF-2nd-Edition-January-2013.pdf

However, by pulling key themes from the learning outcomes within the AQF descriptors, the primary differences between bachelor degrees and advanced diplomas can be illustrated. This is shown in Table 1 below.

Paraprofessional or professional?

One of the most profound issues with advanced diploma standard can be seen in the definition of "paraprofessional":

"a person to whom a particular aspect of a professional task is delegated but who is not licensed to practise as

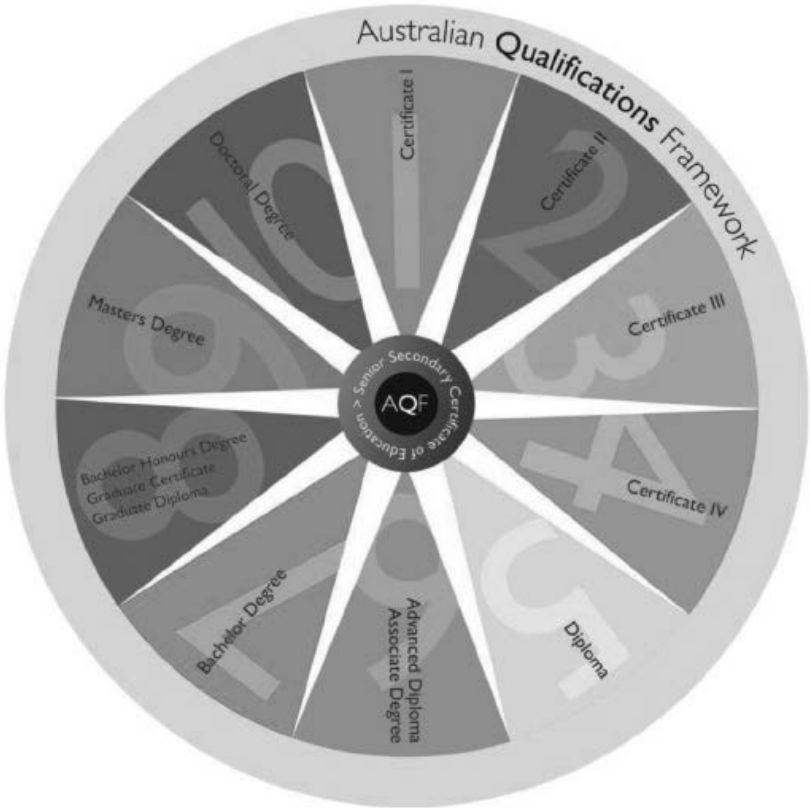

Figure 1: The AQF levels and qualifications wheel (Australian Qualifications Framework 2013)

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a fully qualified professional" (Oxford Dictionary of English 2013).

Herbalists and naturopaths in clinical practice are primarily self-governing and autonomous in their practice. Whilst most naturopaths and herbalists work in collaboration with other health care providers, they don't generally work in a delegate capacity – they are responsible for the assessment of their patients and treatment decisions made in conjunction with the patient. As such the term "paraprofessional" is not truly suitable to describe naturopaths and herbalists, and thus a training standard which aims for this outcome is at best questionable.

Volume of learning – "over-delivering" in naturopathy and herbal medicine training

Perhaps in recognition of the need to produce graduates who are professionals as opposed to paraprofessionals, most private education providers deliver naturopathy and herbal medicine programs which are 2-3 years full time in duration. However, the AQF clearly states that the "volume of learning of an Advanced Diploma is typically 1.5-2 years" (Australian Qualifications Framework 2013). It is likely that this discrepancy will become more of an issue in the next few years as the Community Services & Health Industry Skills Council, as well as the educational providers, will be called upon to justify why these Level 6 qualifications include some Level 7 learning outcomes and why they are "over-delivering" in their qualifications.

Professional association standards

One of the most telling comments on the suitability of the advanced diplomas specified in the Health Training Package is the fact that the primary professional associations (National Herbalists Association of Australia, Australian Natural Therapists Association, Australian Traditional Medicine Society), whilst at various times consulting in the formation and modification of the HTP, have each adopted their own educational standards.

During the early 2000's, the National Herbalists Association of Australia (NHAA) commenced a project to update their course accreditation system. During this period I held the position of Coordinating Examiner on the NHAA Board of Directors, and led the project under the oversight of the president and vice-president. The first step was to identify whether or not the NHAA should simply adopt the Health Training Package standards as the minimum course accreditation standard. After careful review and discussion amongst the examiners and the board as a whole, it was decided that the NHAA could not in good faith accept the HTP as the minimum standard. We identified considerable weaknesses with both the content and the approach of the relevant advanced diplomas, and realised that to adopt these as the NHAA standards would be to move away from one of the key goals of the NHAA – ensuring the integrity of the profession.

Unfortunately, this meant that educational providers delivering these advanced diplomas faced the difficult task of juggling the requirements of both the HTP and professional associations as well as their own internal business requirements.

The argument for higher education

It seems that in general there is agreement within the profession that we want graduates of naturopathy and herbal medicine training to:

- exhibit the characteristics of professionals, not paraprofessionals;
- be autonomous clinicians who collaborate with, but don't necessarily work under, the direction of other health professionals;
- be capable of critical reasoning and intellectual independence, not just highly skilled work;
- have met the standards of professional associations, which are often higher than or somewhat different to

Table 1: Key themes from the AQF descriptors, illustrating the difference between advanced diploma and bachelor degree qualifications

	Advanced Diploma	Bachelor Degree
Type of work	Advanced skilled or paraprofessional work	Professional work
Application of knowledge & skills	Application of specialised and technical knowledge and skill. Work "with some direction" when initiative, judgement, planning or management functions are required.	Application of specialised and technical knowledge and skill, but "with depth in the underlying principles and concepts in one or more disciplines as a basis of independent lifelong learning". "Responsibility and accountability for own learning and professional practice". Critical thinking; solves problems with "intellectual independence". "Well developed judgement and responsibility in contexts that require self-directed work and learning". Works "in collaboration with others".
Course duration	1.5 – 2 years	3 – 4 years

Words and phrases in quotes are pulled directly from the AQF (Australian Qualifications Framework 2nd Edition. January 2013. p15-16. http://www.aqf.edu.au Accessed 30 March 2013)

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the HTP standards;
- have undergone at least 2 (and many would say 3) years of full time study.

All of these requirements are far more closely aligned with Level 7 (bachelor degree) than they are with Level 6 (advanced diploma). It is a clear argument for bachelor degrees to become the minimum standard. Redefining Level 6 in the AQF to meet our profession's requirements is of course out of the question. It is also likely that continued over-delivery within advanced diplomas will be progressively frowned upon by national educational accrediting bodies such at the Australian Skills Quality Authority (ASQA). In light of the inherent limitations of the advanced diplomas and their suitability for our profession, it seems that the next step is higher education.

Changing the status quo

The fact remains that the advanced diploma is still the minimum entry-level qualification to the profession of herbal medicine and naturopathy and it is estimated that only 43% of Australian naturopaths have a bachelor degree (ARONAH 2013).

There is a great deal invested in the current advanced diplomas. There are a large number of providers across the country offering this level of qualification and probably many thousands of students currently enrolled in those courses. The administrative systems, compliance requirements, teaching staff competencies and delivery methods of most private colleges have all focused on the requirements of the Vocational Education & Training (VET) sector, currently governed by ASQA.

A move to bachelor degrees as the standard does not necessarily mean that herbal and naturopathic education becomes the domain of universities only. As an academic who was involved in the University of Western Sydney's Naturopathy program for six years, it is my personal opinion that the university sector as it exists today is the wrong educational and business model for clinical undergraduate courses in naturopathy or herbal medicine. The recent closure of every single Australian university-based clinical qualification in naturopathy or herbal medicine – including some which for years were highly regarded within the profession – seems to add weight to this opinion.

Private educational providers are likely to remain the primary institutions offering clinical qualifications for the foreseeable future. Yet this does not restrict them to only offering advanced diplomas – private bachelor degrees are an acceptable part of the Australian Higher Education sector. However, this means considerable change for providers currently working in the VET sector. Higher education brings with it a whole different set of compliance requirements, delivery methods and administrative and reporting systems, and a different national educational accreditation body – in this case Tertiary Education Quality Standards Agency (TEQSA).

In conclusion – where to from here?

Reflecting on Jean Piaget's opinion on the role of education, we come back to the need for graduates to be able to move knowledge forward and do new things, to be critical and verify, and not just repeat the actions of others. Our current minimum standard of advanced diploma, as defined in the AQF, fails to meet this goal. Whilst the long history of over-delivery goes someway to mitigating this failure, it is questionable whether this over-delivery will be allowed to continue.

With professional associations being the only real governing bodies in our currently self-regulated profession, they are the ultimate determinants of minimum educational standards. In my opinion, it is time for those associations to embrace the AQF and elevate their minimal educational requirements to bachelor degree level. It cannot be done overnight; it should include consultation with private educational providers and other stakeholders, and arguably should embrace an appropriate phased introduction period. But now is the time for our associations to step up and capture the evolutionary "wind" in herbal and naturopathic education and steer the correct course, ensuring the standards for the professional future we believe in and strive to make a reality.

Potential conflict of interest declaration

Ian currently works as Program Manager – Natural Therapies at the Australasian College of Natural Therapies (ACNT), managing the Advanced Diplomas of Naturopathy and Western Herbal Medicine. He was recently a member of the Course Advisory Committee for Bachelor of Health Science (Naturopathy) and Bachelor of Health Science (Western Herbal Medicine) for Southern School of Natural Therapies (SSNT). Both ACNT and SSNT are owned by the THINK Education Group, whose nine different colleges offer both vocational and higher education qualifications in disciplines ranging from health and wellness to hospitality, design and business.

The views presented in this article are those of the author and do not necessarily represent the official views of the THINK: Education Group.

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A naturopathic approach to the treatment of children with autism spectrum disorder: combining clinical practicalities and theoretical strategies

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Abstract: Autism spectrum disorder is affecting an increasing number of children and is multifactorial in its aetiology, pathophysiology and treatment. Natural medicines to date have limited research in this area. Sound evidence does exist for some natural therapies, but many others which may have therapeutic application lack specific research in children with autism. Therapies that have clinical research in disorders with similar underlying pathophysiology may also be beneficial. Further research is necessary into dietary approaches, nutritional supplementation and herbal medicines that may have therapeutic benefit for children with autism spectrum disorder.

Introduction

Autism spectrum disorder (ASD) is a complex condition involving multiple bodily systems. It affects social interaction, communication, sensory perception, development, concentration, attentiveness and learning outcomes. At present, it can be considered a disorder which is genetic, neurological, developmental, immunological, gastrointestinal, musculoskeletal, metabolic, pro-inflammatory and pro-oxidant. As such, defining an evidence based treatment approach has inherent difficulties. Many therapies that theoretically may be useful have yet to be studied. Other therapies that have traditional application for various elements of this disorder lack specific scientific validation in ASD.

Table 1: Key therapeutic issues in ASD

Issue	Clinical Research	Clinical Outcome
Incidence	Incidence of ASD is rapidly increasing at rates greater than can be explained by improvements in diagnosis. Current studies suggest this may be as high as 1-2% (London 2007)	Increased number of children requiring support.
Neuro-transmitters	Hyperserotonaemia in 25-40% of children with ASD; dopaminergic imbalances are common; reduced GABA production and down-regulation of GABA receptors (Aldred 2003, Kidd 2003).	Increased rates of anxiety and depression; impulsivity; reduced inhibitory responses.
Neurological differences	Increased number of neurons in the cerebral cortex; decreased number of neurons in the cerebellum; decreased activity in temporal lobe; reduced global connectivity (Wagner 2006, Vaccarino 2009); inability to filter out background sensations (Shandley 2010).	Developmental delays; slower processing speed; transition difficulties; language difficulties; sensory processing disorder. Enhanced memory or splinter skills alongside impaired social cognition and executive function.
Oxidative Stress	Raised markers of oxidative stress; raised levels of inflammatory cytokines; lower levels of systemic antioxidants (McGinnis 2004).	Higher rates of gastrointestinal inflammation; hyperpermeable blood brain barrier; raised inflammatory mediators in the brain; increased potential for neurodegeneration and demyelination.
Allergies	42% children with autism have C4B null allele (Mostafa 2008).	Higher incidence of autoimmune and allergic disease.
Gastro-intestinal hyper-permeability	Increased rates in children with ASD	Higher incidence of dietary allergies and intolerances; raised inflammation.
Lactase deficiency	Lactase deficiency in up to 58% of children with ASD ≤5 years old (Kushak 2011).	Lactose intolerance.
Familial patterns	Parents with one ASD child have a 27% chance of having a subsequent ASD child; neurotypical siblings are more likely to exhibit language delay, behavioural difficulties, or some degree of subclinical ASD symptoms (Tomeny 2012, Constantino 2010).	Family stress levels can be extremely high. Parental separation is twice as likely with an ASD child (Hartley 2011, Baeza-Velasco 2013).

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Table 2: Summary of evidence for specific therapies for the treatment of ASD in children

Therapy	Rational & Evidence	References
Gluten-free casein-free (GFCF) diet	A high incidence of gastrointestinal malabsorption and gastrointestinal symptoms has been observed in children with ASD. Improvements in core autistic behaviours have been noted in studies with strict adherence to diet over a long period of study (8-24 months).	Whiteley 2010
	Reduced gluten and casein diet did not demonstrate improvement.	Harris 2012
	3 month elimination of gluten and dairy did not demonstrate improvement.	Johnson 2011
	A survey based study found that 83% of parents of ASD children implementing a GFCF diet at the time of the survey reported improvement.	Winburn 2013
	Authors note: there are inherent difficulties in blinding a GFCF diet, as well as difficulties with compliance if adequate food substitutes are not provided. This may contribute to inability to replicate a consistent result.	Adams 2008
Vitamin C	Pilot study reported reduced symptom severity over 10 week study period, consistent with theoretical dopamine potentiating effect of vitamin C.	Dolske 1993
Multi-vitamin & mineral supplement	Demonstrated improvements in sleep outcomes and gastrointestinal symptoms.	Adams 2004
Vitamin B6	Involved in multiple metabolic pathways and is a co-factor for 113 enzymes. High dose vitamin B6 (100-600mg/day) has been shown to improve mental and physical function in ASD.	Adams 2006 Bihari 2006 Pfeifferi 1995
Magnesium & vitamin B6	Red blood cell magnesium has been observed to be lower in children with ASD.	Meletis 2007
	Magnesium (6mg/kg/d) and B6 (0.6mg/kg/d) in children with ASD demonstrated significant improvement.	Meletis 2007
Folate & vitamin B12	Reduced methylation capacity and increased oxidative stress have been observed in patients with ASD. 75mcg/kg injected methylcobalamine combined with 400mg folinic acid daily for 3 months demonstrated significant improvement in behavioural symptoms.	James 2009 Bertoglio 2010
Carnosine	Antioxidant; appears to enhance frontal lobe function; neuroprotective.	Meletis 2007
	800mg L-carnosine per day resulted in significant improvement in behaviour, communication and social ASD traits.	Chez 2002
Omega 3 fats	EPA and DHA are required for neurological development and neuroplasticity. To date, studies are variable and those producing a positive result consist of small groups. Two meta-analyses have reported that there is little quality evidence to support the use of omega 3 fats in ASD.	Bent 2009 James 2011
	Significant improvement was demonstrated in a small pilot study using 840mg EPA, 700 mg DHA, 7mg vitamin E. Improvements included reduced inappropriate speech (39%), stereotypy (72%) and hyperactivity (71%).	Amminger 2007
Exercise	Exercise programs have demonstrated improvements in motor skills, social skills, communication skills, self-efficacy, self-confidence, sensory receptivity and attentiveness. Studies generally consist of small cohorts, and were not blinded.	Bass 2009 Cawley 1994 Pan 2010 Rosenthal-Malek 1997 Sowa 2012 Todd 2010
Acupuncture	Meta-analysis demonstrated improvements in secondary outcomes but not primary outcomes. Secondary outcomes included improved communication, linguistic ability, cognitive function and global functioning.	Cheuk 2011
Animal assisted therapy	Studies have demonstrated that a pet may help a child develop empathy, consideration of others' feelings and self-confidence. Prosocial behaviours have been observed upon introduction of a pet to a family with an ASD child. These behaviours include offering comfort and offering to share.	Adams 2010 Law 1995 Grandgeorge 2012

While clinical therapies should have a sound evidence base, either traditional or scientific, there is potential to limit therapeutic outcomes by restricting therapy to this ideal. This paper will explore the evidence for therapies that may have clinical application in ASD, often drawing upon research into other conditions. A summary of key therapeutic issues in ASD are listed in Table 1.

While many herbal medicines, dietary regimes and nutrients lack sufficient research to support their use in autism spectrum disorder, some have been studied

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extensively. These therapies, however, should by no means be the only treatments used in autism as they do not address all therapeutic concerns. Additionally, some therapies studied in autistic children have inconsistent results. A summary of complementary therapies with specific research in children with ASD is included in Table 2.

In addition to the above therapies with specific evidence to support clinical efficacy, an understanding of the pathophysiology of ASD can be used to explore other therapies that may be of benefit.

Key issues in autism spectrum disorder and potential natural therapies

Gastrointestinal inflammation

Gastrointestinal disease occurs with increased frequency in children with ASD. Russo and Andrews (2010) demonstrated that autistic children were almost seven times more likely to suffer gastro-oesophageal reflux, twice as likely to suffer chronic diarrhoea, three times as likely to suffer constipation, and nine times more likely to suffer irritable bowel syndrome (IBS), than their non-autistic siblings. Furthermore, Krigsman et al (2010) found ileal and/or colonic inflammation present in 74% of autistic children with gastrointestinal symptoms upon diagnostic ileocolonoscopy. Intestinal hyperpermeability has also been observed in autistic patients (Li 2005, Bihari 2006). Identifying and appropriately treating causes of gastrointestinal inflammation is of vital importance from a naturopathic perspective.

Dietary allergy has been identified as a common cause of gastrointestinal symptoms in autistic children. Improvements in gastrointestinal and behavioural symptoms were observed in autistic children on a gluten-free casein-free (GFCF) diet over an eight to twelve month period (Whitely 2010). Similar improvement was not observed for patients on a reduced-gluten diet, nor was improvement observed in a trial of only three months duration (see Table 1) (Harris 2012, Johnson 2011). Other dietary allergies and intolerances also need to be explored and eliminated. A 2008 study found that 52% of autistic children had at least one type of allergic disease and that severity of allergy correlated with severity of autism (Mostafa 2008). Furthermore, exposure to pollen in atopic children with autism has been associated with neurobehavioral regression (Boris 2004).

Healing the gastrointestinal tract: potential therapies in children with ASD

Probiotic therapy Two specific probiotic organisms have been demonstrated to enhance recovery of the intestinal epithelium: Lactobacillus rhamnosus GG and Saccharomyces boulardii (Biocodex strain). Supplementation with L. rhamnosus GG has been shown to produce an anti-inflammatory effect and mediate homeostasis of intestinal epithelial cells (IECs) (Lebeer 2012). A human study conducted in 1996 demonstrated that Saccharomyces boulardii (S.b.) positively influenced the intestinal architecture. Seventy-five percent of subjects showed an increase in surface area of intestinal villi, while twenty five percent had a decrease. Increased brush border enzyme activity was observed, specifically with regard to improved lactase production in subjects who had measureable lactase activity prior to treatment. This effect was not observed in subjects who had no prior lactase activity (Jahn 1996). Furthermore, S.b. has been shown to promote recovery of the intestinal mucosa, following Giardia infection when supplemented over a thirty day period (Guillot 1995). This is relevant for children with ASD considering the higher incidence of lactose intolerance, intestinal inflammation and other intestinal abnormalities identified in this population.

Glutamine Glutamine has been shown consistently to decrease intestinal permeability, reduce intestinal inflammation and improve intestinal morphology (Quan 2004, Benjamin 2012, Vermeulen 2011). Glutamine is considered a non-essential amino acid. It has been extensively studied for post-operative recovery, cancer cachexia and Crohn's disease (Benjamin 2012, Miller 1999). While there is no direct research to support the use of glutamine in ASD, it is potentially useful given that intestinal hyperpermeability and inflammation are key issues for ASD patients.

Herbal demulcents Marshmallow (*Althaea officinalis*) and slippery elm (*Ulmus fulva*) powder may also be useful in reducing intestinal inflammation in ASD patients. Both of these agents have been traditionally used to soothe gastric irritation and inflammation (Grieve 1931). The application of these two herbs in children, however, may be limited by inherent difficulties of compliance. Marshmallow and slippery elm as powders absorb fluid and become a slimy semi-solid mass. In children who can swallow capsules, this should not be a problem. However, in younger children, the texture of these powders may pose difficulties. Parents may need to experiment with different ways of disguising or blending the powder, either in smoothies or mashed into food.

Nutritional intake Nutritional intake can be quite limited in children with ASD. Food "fussiness" is common, as are dietary allergens (Cermak 2010). Nutritional counselling is important with these patients to ensure they have an adequate nutritional intake of all macro and micronutrients. Whitely et al (2010) compared the nutritional intake of ASD children with neurotypical children and found that macro and micro nutrient intake were similar. However, inadequate dietary intake of vitamins A, B6, C and folic acid, as well as the minerals calcium and zinc, have been reported in other studies (Xia 2010). Plasma levels of specific nutrients in children with ASD have been shown to be low, including folic acid, zinc, magnesium, selenium and vitamins A, B6, C, E and D (McGinnis 2004). A thorough diet

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history should be taken with these patients, followed by discussion with the parent as to creative ways to improve nutritional intake. In patients with additional problems of malabsorption, intestinal hyperpermeability and inflammation, supplementation may also be warranted. A comprehensive multivitamin and mineral supplement may be a useful adjunct to support the nutritional needs of growth and development.

Anxiety and depression

Anxiety and depression are prevalent in children with ASD. Current research suggests that up to 84% of people with autism will experience problems with anxiety (Davis 2011, White 2009) and 50% will suffer depression (Teirney 2004). Furthermore, 45% will meet the criteria for ADHD (Skokauskas 2012) and 10% will meet the criteria for obsessive compulsive disorder (OCD) (Gjevik 2010). Sensory overload and sensory defensiveness contribute to anxiety levels being higher in autistic children than neurotypical children (Curtis 2010). Sensory overload occurs because ASD children typically lack the ability to filter out background sensory information and become overwhelmed (Shandley 2012). This sensory input involves all of the senses: smell, taste, sight, sound, touch and proprioception. Furthermore, children with ASD may have dysregulated processing of one or more of these senses. The result of this is that they typically need more time to process information and have greater difficulty formulating responses. Raised anxiety levels may also result in inappropriate responses, violent outbursts or emotional distress when social interactions are difficult, unsuccessful or exceed their skill base. Supporting the nervous system through nutrition and herbal medicines (see Table 3) may be beneficial.

Magnesium Magnesium has been studied in the treatment of anxiety. Magnesium levels have been observed to be lower in children with ASD (Meletis 2007). Grases et al (2006) examined the relationship between exam stress in chemistry students and magnesium. This study found that raised anxiety levels correlated with raised magnesium excretion via the kidneys and lower plasma magnesium levels (Grases 2006). Furthermore, animal research has demonstrated that magnesium deficiency enhances anxiety related behaviour in response to stressful events (Sartori 2012). Supplemental magnesium has been shown to have a positive effect in 70% children with autism at a dose of 6mg/kg/d combined with vitamin B6 (0.6mg/kg/d) (Meletis 2007). Significant clinical improvement of anxiety symptoms has also been demonstrated using magnesium in combination with *Crataegus oxyacantha and Eschscholtzia californica* (Hanus 2004).

Vitamin D Serum levels of vitamin D have been observed to be significantly lower in autistic children compared to healthy neurotypical children (Meguid 2010, Molloy 2010, Mostafa 2012). Mostafa and Al-Ayadhi (2012) found that 40% of a population of autistic children were vitamin D deficient and a further 48% were vitamin D insufficient. Additionally, auto-immune antibodies have been shown to be significantly raised in 70% of autistic children and in 90% of children with severe autism (Mostafa 2012). Vitamin D deficiency has also been correlated with increased incidence of autoimmunity and allergic disease (Jones 2012). Vitamin D is involved in regulatory mechanisms of the immune system, as well as the production of inflammatory mediators (Jones 2012). Current research suggests that auto-immune antibodies and inflammatory mediators are involved in the pathogenesis of autism in-utero and remain significantly raised lifelong (Zimmerman 2008).

Vitamin D deficiency is also associated with increased incidence of anxiety, depression, lowered cognitive function (Wilkins 2009), psychosis and increased suicide risk (Tariq 2011). Supplementation of vitamin D has been shown to improve mood in seasonal affective disorder (Lansdowne 1998). Studies examining the relationship between vitamin D supplementation and depression have to date been variable, and while dosage amounts range substantially, even studies using comparable amounts were inconsistent (Li 2013).

Vitamin D is able to cross the blood-brain-barrier (Li 2013) and is involved with neuronal development and connectivity (Mostafa 2012). Vitamin D has an integral role in key areas of autistic pathophysiology. While studies regarding supplementation lack consistency, research suggests that vitamin D deficiency may adversely impact autistic presentation and should therefore be addressed.

Herbal medicines for anxiety and depression Herbal medicines should also be considered as part of the treatment of anxiety and depression in autistic children. The herbalist, however, must consider taste and other compliance issues when mixing liquid herbal medicines for children. In older children, tablets or capsules may be used, although this limits the individualisation of prescriptions. Table 3 contains a list of herbal medicines that could be considered, along with their potential therapeutic benefits. This list is by no means exhaustive; many other herbal medicines may be used to support specific therapeutic goals on a case by case basis.

Zinc, copper, selenium and heavy metals

There is research to suggest that zinc levels are consistently low in autistic children (Faber 2009, Bjorklund 2013). Zinc deficiency may result from malabsorption in the gastrointestinal tract or inadequate dietary intake. Furthermore, zinc deficiency negatively impacts upon appetite and taste perception, which may further limit nutritional intake. Zinc may play a large role in the 'food fussiness' and feeding difficulties reported by many parents of children with autism. Excessive copper levels have also been observed in autistic children (Bjorklund 2013). Disordered metallothionein function appears to be implicated in abnormal zinc:copper ratios

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Table 3: Potential herbal medicines for the treatment of anxiety and depression in children with ASD

Botanical name	Common name	Traditional Use	Taste considerations
Avena sativa	Oats green	Relaxing nervine, thymoleptic	Mild taste. Caution in coeliac disease or gluten intolerance
Bacopa monniera	Bacopa; Brahmi	Anxiolytic, improves memory and concentration	Mild, sweet. Caution: may cause gastric irritation and diarrhoea
Codonopsis pilosula	Codonopsis	Adaptogen, improves appetite, aids digestion	Mild and sweet, high dosage range
Eschscholtzia californica	Californian poppy	Anxiolytic, sedative, anodyne	Unpleasant, but can be disguised by other sweeter or more flavoursome herbs
Hypericum perforatum	St John's wort	Antidepressant, anxiolytic, nerve tonic	Mild taste, easily disguised
Lavandula angustifolia	Lavender	Antidepressant, anxiolytic, carminative	Bitter in isolation, combines well with other aromatic herbs
Leonurus cardiaca	Motherwort	Anxiolytic, thymoleptic	Bitter, difficult to disguise taste, currently unavailable as tablet in Australia
Matricaria recutita	Chamomile	Anxiolytic, mild sedative, carminative	Mildly bitter, aromatic. Pleasant as a tea diluted with apple juice, combines well with other flavours
Melissa officinalis	Lemon balm	Anxiolytic, thymoleptic, carminative, improves memory and concentration	Mild and pleasant as both tea and tincture; masks taste of less pleasant herbs
Nepeta cataria	Catnip	Anxiolytic, sedative, carminative	Mildly aromatic, pleasant tasting
Ocimum tenuiflorum	Tulsi; Holy basil	Anxiolytic, thymoleptic, improves memory and concentration, antioxidant	Aromatic, pleasant tasting
Passiflora incarnata	Passionflower	Sedative, anxiolytic, anodyne	Mild tasting
Piper methysticum	Kava	Anxiolytic, anodyne, sedative, muscle relaxant	Mild tasting
Rosmarinus officinalis	Rosemary	Antioxidant, carminative, improves memory and concentration, circulatory stimulant	Aromatic, but not unpleasant tasting
Scutellaria lateriflora	Scullcap	Anxiolytic, sedative, nerve tonic	Bitter
Valeriana officinalis	Valerian	Anxiolytic, sedative, muscle relaxant	Pungent taste and smell
Withania somnifera	Ashwaghanda; Winter cherry.	Adaptogen, sedative, anxiolytic	Mild tasting

(Kidd 2002, Faber 2009). Furthermore, heavy metals lead and mercury have been observed to be high in children with autism, while magnesium and selenium have been measured to be significantly low (Lakshmi 2011). The presence of raised heavy metals, and lowered zinc, selenium and magnesium appear to be correlated with increased autism severity (Lakshmi 2011). Supplementation of zinc, magnesium and selenium may therefore be warranted in children with autism.

Supporting neurological development.

Many studies have demonstrated that there are distinctive differences when comparing the brains of autistic patients with those of neurotypical patients. The autistic brain has a greater number of neurons in the cerebrum, fewer neurons in the cerebellum and shows less connectivity between different sections of the brain (Wagner 2006, Vaccarino 2009). Neurotransmitter levels are also measurably different. Up to 40% of people with ASD have raised serotonin levels; dopaminergic imbalances are also common (Kidd 2003). Additionally the brain is more vulnerable to oxidative damage in patients with ASD due to having a hyperpermeable blood brain barrier (BBB) (McGinnis 2004). Studies have shown that hyperpermeability and inflammation in the gastrointestinal system increase systemic inflammatory mediators, which in turn increase the permeability of the BBB and create raised inflammatory mediators in the brain (McGinnis 2004).

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Essential fatty acids

Many strategies used in the treatment of autism in children, including speech therapy and occupational therapy, rely on neuroplasticity. Neurological structure, function and connectivity are responsive to stimuli, activities and training (Mundkur 2005, Doman 2008, Cramer 2011). New neural extensions and connections can be encouraged by specific repetition of desired activities or behaviours in preference to less desirable activities or behaviours. Omega 3 fatty acids, EPA and particularly DHA, are essential for maintaining high neural membrane fluidity which is ideal for neuroplasticity (Kidd 2007). However, published research regarding the therapeutic benefit of omega-3 fatty acids has shown inconsistent results to date. Inherent difficulty exists in interpreting existing research due to small cohort sizes, difficulty in blinding subjects and assessors, and the small doses used in many of the trials. According to two meta-analyses, sufficient evidence is currently lacking to support the use of essential fatty acids in children with ASD (Bent 2009, James 2011).

Turmeric *(Curcuma longa)*

The therapeutic applications of curcumin, the active component in *Curcuma longa* (turmeric), have been well researched and documented. Curcumin is a potent antioxidant and anti-inflammatory, and has immune modulating effects (Gupta 2013). Curcumin has been demonstrated to have an anti-inflammatory effect in many gastrointestinal disorders, including Crohn's disease, inflammatory bowel disease, irritable bowel syndrome, peptic ulcers and non-specific gastric inflammation (Hanai 2009, Baliga 2012, Gupta 2013). It has also demonstrated anti-inflammatory effect in chronic inflammatory conditions such as cancer, arthritis, cardiovascular disease, uveitis, vitiligo, psoriasis, atherosclerosis, diabetes and diabetic nephropathy (Gupta 2013).

Curcumin reduces inflammation through several mechanisms, including the down-regulation of production of inflammatory transcription factors and pro-inflammatory cytokines, and its impact on oxidative stress (Shehzad 2013). Curcumin is safe, non-toxic and well tolerated (Baliga 2012, Gupta 2012, Hanai 2009, Noorafshan 2013, Shehzad 2013). Curcumin has very poor bioavailability as it has low gastrointestinal absorption, is rapidly metabolised and is rapidly excreted (Gupta 2013). Adjunctive therapies can improve bioavailability. Piperine, the major alkaloid in *Piper nigrum* (black pepper) has been shown to increase absorption of curcumin by 2000% (Dudhatra 2012). Clinical caution must be exercised, however, as piperine may also increase the absorption of other nutrients and some medications (Dudhatra 2013). Clinical trials conducted on Meriva® (Indena S.p.A, Milan), a patented complex combining curcumin with phosphatidylcholine, also found a 2000% increase in absorption via oral administration (Belcaro 2010). This extract may have broader therapeutic application as it can be confidently be used alongside most pharmaceutical medications.

Given the inflammatory nature of autistic pathophysiology systemically, in the gastrointestinal tract and specifically in the brain, curcumin has multiple potential therapeutic benefits. Curcumin is able to cross the blood brain barrier and has specific effects on neurogenesis and the production of neurotransmitters norepinephrine, dopamine and serotonin (Kulkarni 2009). Curcumin has a potential role in the treatment of depression and other inflammatory conditions in autism, as well as being a supportive adjunct to therapies that utilise neuroplasticity. Curcumin has a well demonstrated safety profile and is bioavailable when combined with piperine or with phosphatidylcholine in the patented product Meriva®.

Oxidative stress

Oxidative stress may play a key role in the pathogenesis and behavioural difficulties present in children with ASD (McGinnis 2004). Oxidative stress occurs when oxidants exceed the functional capacity of anti-oxidants and results in free radical damage to tissues and functional impairment (McGinnis 2004). Studies examining the plasma levels of anti-oxidants present in the serum of autistic children have demonstrated lower levels than those present in neurotypical children (Frustaci 2012). Anti-oxidant supplementation may help reduce oxidative stress and should be considered in children with autism. This could be through anti-oxidant rich foods in the diet or specific supplementation.

Clinical considerations: sensory overload and sensory defensiveness

When treating people with autism, it is important to consider the clinic space and how it might appear to someone with heightened and unfiltered sensory perception. This includes lighting levels, clutter, smells and background noises. Awareness also of the clinician's own behaviours, perfume, deodorant and clothing must also be considered. Finding practical ways of limiting sensory input may help reduce stress and anxiety for the autistic patient and be conducive to a therapeutic relationship.

Communication

Communication can be quite challenging for children with autism, even those who are high functioning. Direct communication with the patient will vary based on age and language competence. The patient may struggle with a stutter, may rely heavily on echolalia or may be non-verbal. Language interpretation is typically quite literal, therefore it is important to use clear concise communication and avoid the use of colloquial phrases. It is important to monitor the stress levels of the patient

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and limit the duration of the consultation based on individual needs. Positive therapeutic relationships should foster acceptance of the patient, while being mindful of individual challenges and talents. One should be protective of the patient's self-esteem in the way they are discussed. It is important to praise any progress (for both parent and child), particularly with difficult milestones, and to find positive ways to explain the goals of the treatment regime.

Further research

Clearly there is need for further research into the therapeutic potential of herbal medicine, dietary intervention and nutritional supplementation for children with autism. Parents seem motivated to participate in clinical trials to improve research-based knowledge in this area (Adams 2008), though parental reluctance has been observed with the blinding of these trials (Winburn 2013). A survey-based study found that 78% of parents of ASD children said that they would consider being part of a randomised controlled trial; of this group, 45% said they would be more likely to participate if the study was not blinded (Winburn 2013). Early intervention in autism has a critical impact on life-long outcomes (Tierney 2004, Matson 2009). As such, being within the control or placebo group may be seen by these parents as valuable therapeutic time lost. Many parents will use the Internet to search for therapies for their children, though they will often lack the skill to critically assess the information they find. It is arguably unreasonable to expect parents to delay potential treatments while we wait for the research to catch up. The clinician can potentially approach this dilemma by employing therapies that have clear therapeutic benefit and demonstrated safety in related disorders with similar underlying pathologies.

Conclusion

Natural therapists have the potential to support the health, growth, development and learning outcomes of children with autism. This may be through dietary intervention, nutritional supplementation or herbal medicines. With recent increases in the incidence of autism, research into the efficacy of natural medicines is extremely important. Some natural therapies have been extensively studied. Other natural therapies, while theoretically useful, have yet to be studied specifically in autistic children. Further research into natural medicines with demonstrated clinical efficacy in disorders with similar pathophysiological processes is therefore necessary.

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To the editor *continued from page 163*

cohesive group and firmly establish a place within the Australian health care system? I believe there is a strong place for naturopaths and Western herbalists and that the Australian public values the service we provide, and appreciates and respects our holistic approach. However, unless we can collect ourselves, identify and address areas of deficiency and build our strengths, we are at risk of becoming obsolete and superfluous as other registered health professions and indeed the retail supplement industry move into our territory. Critical thinking and intelligent debate is fundamental and it starts with critical thinking about ourselves and our profession. To quote my insightful Clinical Studies teacher, Dr Karen Bridgeman, "It is difficult to regulate (or aggregate) a group of people whose main aim is to be alternative." It is essential that we are able to come together, to sensibly debate issues at hand, and to rely on our own resources as intelligent professionals rather than remain disparate and vulnerable to marketeers with their own commercial interests. Thanks again to Dr John Wardle for raising the debate – I appreciate the opportunity to contribute, and look forward to hearing the views of others.

Susan Arentz
Arncliffe NSW

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Anthroposophic Medicine: deepening our understanding of herbs, healing and the human being

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Abstract: Anthroposophic Medicine is a European-based model of medicine founded by the Austrian scientist and philosopher, Rudolf Steiner, around 100 years ago. Anthroposophic medicine aims to increase our understanding of the human being and medicinal substances and serves to bring together ancient medical wisdom with modern scientific research. This article will explore the foundation concepts of this comprehensive and dynamic model of medicine, which are surprisingly relevant and applicable to the modern setting with particular reference to herbal medicine.

"Real medicine can only exist when it penetrates into knowledge which embraces the human being in respect to body, soul and spirit."
Rudolf Steiner

The evolution of our understanding of the human being and the subtle forces that permeate life has been increasing in recent years with insights from quantum science. Historically, many Western practitioners have turned to the ancient healing traditions such as Ayurveda and Traditional Chinese Medicine to enrich and complement the scientific approach to medicine, which often falls short of treating the whole person. Anthroposophic Medicine (AM) is a European-based model that may deepen our understanding of the human being, herbal medicine and healing. AM is a comprehensive model that includes both Western and Eastern philosophical principles, bringing ancient medical wisdom together with modern scientific research. Despite being founded around 100 years ago, it is surprisingly relevant and applicable to the modern setting. Indeed, some of the new quantum science discoveries brought to light over recent decades are surprisingly similar to what Rudolf Steiner first proposed at the turn of last century.

Rudolf Steiner (1861-1925) was an Austrian philosopher, scientist, spiritual teacher and esotericist. Steiner studied widely including the natural sciences, botany, chemistry and physics. He was influenced by many different thinkers in developing his original ideas, one of the most notable being the philosopher and naturalist Goethe (1749-1832). Rudolf Steiner developed a framework for understanding the human being and our unique relationship and interconnectedness to the macrocosm and microcosm of the universe. This framework is known as *anthroposophy*. Steiner applied the anthroposophic philosophy to a range of fields, with the most well-known applications being in the fields of education (Steiner or Waldorf schools) and agriculture (biodynamics – a holistic organic approach to gardening and farming that utilises a number of preparations indicated by Steiner, some of them made from medicinal plants).

The development of a medical tradition of anthroposophy was born when Steiner presented a series of lectures given in 1920 to a group of doctors in English, commonly referred to as the *First Medical Course*. As Steiner was not a trained medical doctor, he also collaborated with Dutch physician Ita Wegman in the development of AM. He also further developed teachings from a range of influential philosophers and thinkers within medical history, including Paracelsus (1493-1541) and Hahnemann (1755-1843). For instance, Steiner used the Paracelsian alchemical idea of the *tria prima*, comprising of mercury, sulphur and salt. He endeavoured to understand more deeply the innate nature and quality of these substances and how they could be used in devising remedies.

AM has never aimed to be alternative as it accepts and works with the mainstream conventional medical approach. However, it does not stop at the scientific model but integrates it with another equally important form of knowledge, that of spiritual science. Spiritual science is the application of the scientific method to the human soul-spiritual dimension and related phenomena that fall outside the physical and sense-perceptible world. By incorporating all aspects of the human being it provides a rich and integrated holistic framework. It thus serves to expand our understanding beyond the rational approach in all aspects of medicine from physiology and pathology to medical treatments and therapies.

Understanding anthroposophy

To understand how medicines are prepared and utilised in AM, one first needs a basic understanding of anthroposophy. The word *anthroposophy* comes from *anthropos* (human being) and *sophia* (wisdom) and can

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be translated as "wisdom of the human being" or "human wisdom." Steiner asserted that there were no limits to human knowledge and he emphasized different ways of knowing and a deepening of observational powers beyond the basic senses. As such his methodology is essentially based upon a combination of imaginative, inspired, intuitive and practical intelligences. Fundamentally, anthroposophy respects both intuitive insight and scientific 'truths'.

A basic understanding of the dimensions and layers of the human being according to anthroposophy is essential to understand how AM works (Huseman and Wolff 1982).

Four Fold Human

According to anthroposophy, the human being is comprised of four layers:

- Physical (dense, material body)
- Etheric (vital body)
- Astral (soul/emotional body)
- 'I Am' principle (spirit/higher body) - sometimes called ego.

Three Fold Human

A further three spheres and related processes are seen to govern the functions of the human being. These are somewhat akin to the "head, heart & hara" of many traditions.

- Nerve Sense Sphere: process of thinking
- Rhythmic (Heart/Lung) Sphere: process of feeling
- Metabolic/Limb Sphere: process of willing

The human being can be seen to be composed of an 'upper pole' that processes nervous and sensory functions that are largely conscious processes, and the 'lower pole' that governs metabolism and parasympathetic processes that are largely unconscious. The 'rhythmic system' operating in the middle offers a mediating sphere that serves to balance the catabolism of the nerve sense pole and the regenerative anabolism of the lower gut and limb pole. It is through the domain of the rhythmic system, the breathing and the circulation that the organism strives to maintain health and homeostasis (Steiner 1920).

In an anthroposophic sense, disease is seen in the context of an imbalance between the interplay of the four bodies or an imbalance in the function of the three spheres/poles. For example, a migraine could be related to too much activity in the upper nerve sense pole and an emphasis of astral (soul) body activity (emotional stress and tension). This imbalance gives rise to symptoms including headache and visual disturbance in the upper sphere and digestive disturbances in the lower metabolic pole. The task of the AM practitioner is to determine which layers need to be strengthened, stimulated or moderated to restore harmony in the human being. Therefore, remedies are seen to have an affinity with the different dimensions of the human being and can facilitate and restore balance where indicated.

Philosophy and approach to Anthroposophic Medicine

With an anthroposophic understanding of the human being in place, practitioners view human wellness and illness as reflections of biographical events connected to the body, mind and spirit of each individual. AM also aims to acquaint the patient with the true nature and cause of their illness and the deeper destiny and insight that may be offered through healing. Health is seen as the ability to attain a certain level of flexibility and resilience throughout life and to grow and learn from life's challenges. With this in mind, AM incorporates a range of modalities that are suited to each individual and may include painting therapy, counseling, therapeutic eurythmy (movement), and massage, along with nutritional advice, herbal medicine and homoeopathy. Application of homoeopathic or phytotherapeutic substances take the form of oral ingestion, injected forms of medicine and external treatments. (International Federation of Anthroposophic Medical Associations n.d)

Anthroposophic nursing is also pivotal to many aspects of AM practice and often involves hydrotherapy – from compresses, wraps and baths to inhalations. It is important to note that in AM there is also a strong emphasis on education being an important part of child health. Moreover, an education that nourishes the whole child is seen to both promote health and be curative for certain health and developmental issues, such as autism spectrum disorders or attention deficit disorder (Glocker 2002). As such, most Steiner schools have a school doctor who works with the teachers to address how to best meet the developmental and health needs of the children.

Understanding the remedies

In AM, four groups (kingdoms) of nature are identified and comprise the mineral, plant, animal and human kingdoms. Remedies can be chosen from any group and are seen to display an ascending complexity. For example, minerals or metals only possess physical matter, whereas plants contain both physical and etheric substance and animals contain physical, etheric and astral qualities.

- Minerals: physical only
- Plants: physical & etheric
- Animals: physical, etheric and astral
- Human: all layers, organ remedies

Medicines are generally taken from the realm of plants, animals and minerals. Medicines are always devised and prepared according to the intricate inter-relationship between human beings and nature – plant, mineral and animal. While conventional diagnostic and prescribing criteria, such as *materia medicae* from homoeopathic and herbal medicine modalities, are used when determining the best substance, there are also key distinctions. One of the differences between traditional natural medicines and AM is in the growing, harvesting and manufacturing principles. Plant remedies are grown

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according to biodynamic principles, harvested with intentionality and according to seasonal, lunar and solar cycles, all of which are thought to help harness additional life forces for the plant remedies. Remedies may be further enhanced through a range of dynamic processes. For example, compared with classical homoeopathy, rhythmical rocking rather than succussing (shaking) is used to potentise a remedy. The lemniscate or vortex may also be used to imprint vibrational forces into the medicinal substance.

Both rational knowledge and intuitive insight is needed when making an assessment and prescribing substances for healing. Questions that need to be addressed might include:

1. Which of the 3 functional systems (nerve sense, rhythmic or metabolic) should primarily be addressed?
2. Which organ is the key?
3. Which substance is needed?
4. Should the medicine be administered in its natural state or should it be transformed through a process that establishes a deeper more effective relationship to the disorder presenting in the human being?

In addition, remedies and therapies are given according to a specific time rhythm depending on what layer is being worked on. For example, the physical body may require a whole year of treatment, while the etheric body responds best to a monthly treatment rhythm. The astral body is given a weekly rhythm in relation to treatments (e.g. art therapy) and the 'I am' (higher spiritual process) is given a daily dose until a response is elicited (Vademecum of Anthroposophic Medicines 2009).

Plants in Anthroposophic Medicine

Many different plants are used in anthroposophical medicinal remedies. When observing plants one might notice that they comprise both physical and etheric substances and forces. Plants take earth energy from the ground and solar energy from the sun and transform it into plant energy, food and medicinal substances. Plants do not possess a soul, or higher 'I' or conscious principle. From an AM perspective, the astral layers of plants exist outside the plant and are not found within the plant.

The etheric force is easy to witness in a plant when you consider how the life force directs both the sap flow and the upward growth habit of plants. Both of these activities of the plant defy gravity, with the plant having to overcome the forces of gravity to emerge from the seed and push through soil to reach the sunlight. The invisible force that keeps a tiny seedling upright and orienting towards the sun is the etheric process.

Goethe

Steiner was inspired by the German writer, artist, scientist and philosopher, Johan Wolfgang von Goethe (1749-1832). Goethe developed a phenomenological approach to science, in particular botany and anatomy, which called upon deepening the human powers of observation. He distinguished between manifestation and essence, stating, "*It is not our senses which deceive us, but our judgment*" (quoted in Van Der Bie, 2003).

Goethe wrote the classic book *The Metamorphosis of Plants* (1790) and in it he discusses the archetypal plant known as the *urpflanze.* From his observation, all plants emerge from the seed, develop a leaf process, then develop a root sphere and flower process. The essence of the archetypal 'plant' is found in the green sphere of the leaf. Steiner applied Goethe's theories and extended them, summarising this approach in his book *Goethean Science* (Steiner, 1883). In turn, Steiner's application in relation to medicine and botany was further extended and interpreted by Oskar Schmiedel (1887-1959) and Wilhelm Pelikan (1893-1981). Schmiedel was instrumental in the development of anthroposophic medicines, in particular through his work at the natural medicine company, Weleda. Pelikan was a pharmacist, AM practitioner and gardener who applied a Goethean approach to observing and using plants. He worked closely with Schmiedel at Weleda and also wrote a book entitled *Healing Plants,* which is essentially an anthroposophic herbal *materia medica.*

The archetypal plant gives us a foundation on which to compare all plants and, in particular, herbs. Observing whether a plant has a dominant leaf process, flowering process or root process will offer insight into the plant's gesture or expression. From a reductionist viewpoint, one might predict that a plant will have more of certain pharmacological constituents if the plant's process is dominant in the root sphere. However, with an AM lens, we can widen the understanding further to see what else the plant reveals about its healing potential.

The human being can be seen to have an affinity with the gesture of the archetypal plant form, but it exists in a reverse polarity. This upside down plant is a model that enlivens the way plants can be seen and used for human healing. The root process corresponds to the head or nerve sense sphere, the leaf process to the rhythmic (breathing and circulatory) system and the flowering/fruiting process corresponds to the digestive and reproductive domain of the human being. It is interesting to note that many flowers and seeds are used in digestive and reproductive disorders, leaves in lung disorders, and roots for nerve complaints.

The following photos demonstrate this relationship in detail. While this system suggests a relationship to the classic Doctrine of Signatures, there is a greater depth to it than just a visual cue.

Rhodiola rosea (Figure 1) and *Valeriana officinalis* have dominant root processes and possess an affinity for the nervous system.

Verbascum thapsus and *Althea officinalis* (Figure 2) have dominant leaf processes, and are used in lung complaints.

Vitex agnus castus and *Matricaria recutita* (Figure 3) both have a dominant flowering and fruiting process

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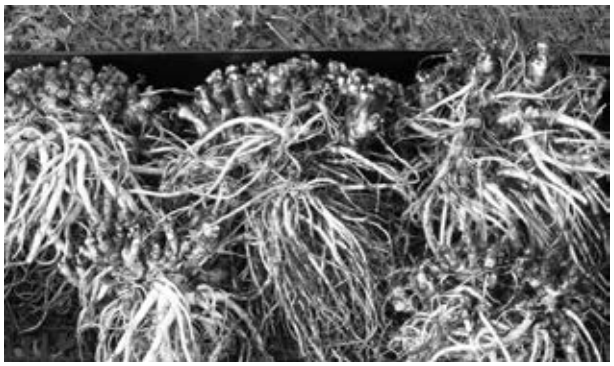

Figure 1: *Rhodiola rosea.* Photo courtesy of Gord Steinraths, Harmonic Herbs.

Figure 2: *Althea officinalis*. Photo courtesy of Kristian Peters and sourced from http://commons.wikimedia.org

and are used for reproductive and digestive disorders respectively.

Many of the medicinal plant genera hold a signature that can be determined through close observation. For example the *Labiatae* (*Lamiaceae*) family are considered plants of warmth, possessing volatile oils and varying degrees of heat, while the *Umbelliferae* (*Apiaceae*) family are plants of air, displaying a delicate ethereal process in their flowering habit and, in many cases, hollow, air laden stems.

Some AM herbal remedies are identified and utilised because of the way certain plants are seen to have affinities with specific minerals. The remedies do not just contain the mineral and a plant extract, but a mineral having been processed, enlivened and harnessed by the plant. These plants have a capacity to take the minerals up from the soil and as such enliven them and create a new vehicle for the mineral to be utilised.

A mineral that ordinarily belongs to the physical plane only is given some etheric

vitality via the plant. A classic example of this is *Urtica dioica* and iron. In anthroposophic medicine, iron is a key mineral remedy and many different forms are used, in particular to harness the higher 'I' principle within the human being. Nettle has the capacity to take iron from the soil and consolidate it and as such it is seen to be a special herb that can be utilised when iron is needed.

Figure 3: *Matricaria recutita*. Photo sourced from http://commons.wikimedia.org

Other examples of plant and mineral affinities include *Melissa officinalis* and copper, *Equisetum arvense* and silica, and *Thuja occidentalis* and silver.

Metamorphosis

According to Goethe, plants take a journey of metamorphosis from the realm of the seed through different growth processes, to flowering or fruiting and then eventually decay. The plant is a living and dynamic life form that is constantly evolving towards further stages of growth and following seasonal cycles. Plants possess different qualities throughout the journey from seed to flowering, and selecting plants at various stages can add a further dimension to the healing attributes.

Elder flowers (*Sambucus nigra)* for example are traditionally used for upper respiratory complaints as they possess anticatarrhal and diaphoretic actions, yet the berries that form from the flowers further develop antiviral and antibacterial compounds (Krawitz 2011). The following pictures of *Echinacea* (Figure 4–7) demonstrate the metamorphosis journey where the plant ends up at decay, but holds within it at this point the seeds that enable the next cycle of new plants.

We can apply and observe the principle of metamorphosis to any dynamic living organism and to human development.

"*When we study metamorphoses we practice 'bringing to light' what is not immediately apparent to the senses. With 'bringing to light' we mean 'making visible for our thinking"* (Van Der Bie, 2003).

The process of expansion followed by contraction that is inherent in metamorphosis is a cyclic rhythm which when studied allows greater insight into the forces that lead to both health and disease processes. The first analysis one might apply involves the senses and perception and the second step is a process that must bring what is perceived to the realm of thought. It is important to refrain from moving straight to the thought and analysis process which, for many of us, is a habit that has to be overcome; instead we need to first apply keen observation through the senses.

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Figure 4: *Echinacea.* Photo courtesy of Zantastik and sourced from http://commons.wikimedia.org

Figure 5: *Echinacea.* Photo courtesy of Arto Alanenpää and sourced from http://commons.wikimedia.org

Figure 6: *Echinacea.* Photo courtesy of H. Zell and sourced from http://commons.wikimedia.org

In conclusion

To understand herbs and their healing qualities from a higher perspective rather than limiting our view of their actions to a mere reductionist approach, we have seen how an anthroposophic lens can provide a useful and in-depth framework. Rudolf Steiner had a heightened imaginative and perceptive capacity and was able to create an all-encompassing and holistic framework that can be applied in diverse fields and many areas of focus. In many respects, Steiner's teachings and insights were well before his time and are just as relevant and needed today.

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Figure 7: *Echinacea.* Photo courtesy of Arto Alanenpää and sourced from http://commons.wikimedia.org

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The alchemy of herbal medicine: spagyric tinctures, elixirs and the vegetable stone

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Abstract: Spagyric tinctures and elixirs represent a traditional herbal manufacturing dosage form that has strong links to alchemy, which is believed by many historians to be the progenitor of modern chemistry. The first to publish extensively on the topic of spagyrics was Phillipus Aureolus Theophrastus von Hohenheim (Paracelsus), who presented the idea of reincorporating the calcined herbal marc back into the herbal tincture. This paper seeks to discuss the evolution of spagyrics and its close links to alchemy, also touching briefly on foundational alchemical concepts to provide a basis of understanding for spagyric development. It will also highlight certain key manufacturing steps that are required in the making of the spagyric tincture, spagyric elixir and the highly prized Lapis vegetabilis (vegetable stone).

Introduction

Herbal medicine has a long history of use dating back approximately 60,000 years (Leroi-Gourhan 1975, Lietava 1992), with actual written evidence documented as far back as the Sumerians (ca. 5400BCE) and Akkadians (ca. 2270-2083BCE) of ancient Mesopotamia (Sinclair & Hechtman 2011, Estes 1989). During this evolving timeframe, multifarious posological formats of herb delivery have been utilised, from raw crude herb taken as a powder or burnt and inhaled, to highly sophisticated standardised extract pro extracts, oxymels, syrups and liquid extracts. Amidst this development, the concept of spagyrics was conceived, which represents an almost forgotten herbal manufacturing method that medieval period writings suggest was first expounded by Paracelsus (1493-1541CE) at a time in history preceding the scientific revolution (1550-1700CE).

To understand the historical development of herbal spagyric tinctures and elixirs, one must first explore some fundamental philosophies of the ancient science of alchemy. Alchemy has been practised in numerous and diverse cultures throughout history, with examples of its practice being found in Indian, Greek, Chinese and Arabic literature (Holmyard 1990). It began its slow infiltration into Europe via the occupation of the Iberian Peninsula by the Islamic Moors, and the various alchemical treatises were translated into languages other than Latin, Arabic and Greek.

Alchemy has numerous definitions that encompass various viewpoints depending on the individual academic authority. From a modern perspective, alchemy has been defined as a "*medieval forerunner of chemistry, concerned with the transmutation of matter, in particular, with attempts to convert base metals into gold…*" (Oxford 2013) or "*a medieval chemical science and speculative philosophy aiming to achieve the transmutation of the base metals into gold, the discovery of a universal cure for disease and the discovery of a means of indefinitely prolonging life*" (Merriam-Webster 2013).

Conversely, the definitions as described from actual practising alchemists are quite different. Alchemy is defined by Frater Albertus (1974) as *'the raising of vibrations…a transmutation*'. In the words of Paracelsus, alchemy '*… is to carry to its end something that has not yet been completed*' (Jacobi 1979) and is a method for '*discerning between the true and the false'* (Paracelsus & Waite 1894). Jabir ibn Hayyan (721-815CE), known as Geber in the West, states that '*this Science treats of the imperfect bodies of minerals, and teacheth how to perfect them*' (Russell 1994). What both ancient and modern interpretations allude to is a single universal substance which can perfect matter, taking something that is vulgar and purifying and perfecting it into something rarified and special. Alchemists called this alchemical substance *lapis philosophorum*, more commonly known as the *philosopher's stone*. However, the application of this knowledge is where modern and alchemical interpretations divide. Modern authorities suggest alchemy simply being used on matter in its diverse crude physical forms; whereas alchemists agree that this can also be taken to refer to the perfection of the human being, therefore also representing a metaphysical or spiritual process toward enlightenment (Eliade 1962, Roob 2009).

The use of the term 'science' in defining alchemy is of great importance, as it posits the use of an evidence-based scientific method that the ancients were utilising centuries before the publication of *On the Revolutions of the Heavenly Spheres* by Nickolaus Copernicus in 1543, which is cited as being the beginning of what we now call the Scientific Revolution. Modern evidence gives support to this with the testing of medical interventions for efficacy by Avicenna in the 11th century, as discussed in *The Canon of Medicine* (Brater & Daly 2000, Daly & Brater 2000), long before the proposed birth of comparable

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randomised clinical trials in 1747 by James Lind (Jallion 2007). If science is defined as '*the intellectual and practical activity encompassing the systematic study of the structure and behaviour of the physical and natural world through observation and experiment*' (Oxford 2013), such a definition either narrows the gap between what we call 'traditional' and 'scientific' evidence, or blurs the lines which divide them.

Etymology

There currently exist two major theories as to the etymology of the word alchemy. Goddard (1999) posits that the Arabic definite article '*Al*' was combined with the word '*Khem/Chem*', an ancient name for Egypt which literally translates as 'black earth' or 'black land". This reference was to the black fertile soil of the Nile delta, which made Egypt a trading and agricultural juggernaut at the time. In contrast, the Oxford dictionary (2013) postulates that the Greek terms '*Khemia'* or '*Chumeia'* (χυμεία) has links to ancient pharmaceutical practices and the '*art of transmuting metals'*. Whilst these theories posit on the etymology of the term 'alchemy', they do not prove that either of these cultures can lay claim to its genesis.

History of alchemy

Of particular interest are the many learned people that have studied alchemy throughout the ages, many of whom laid the foundation for the modern sciences as we currently know them. A short list of key alchemical practitioners is highlighted below in Table 1.

Worthy of note here is Paracelsus, considered a father of modern toxicology; Robert Boyle, considered the father of modern chemistry, inventor of Boyle's Law and author of the *Skeptical Chymist*; Hennig Brandt who discovered phosphorus, and Sir Isaac Newton, who wrote extensively on the topic of alchemy. This fascination with alchemy led the economist J.M. Keynes, who held the largest privately owned collection of Newton's 'Chymical' writings, to say that Newton '*was not the first of the Age of Reason. He was the last of the magicians'* (Royal Society 1946).

The Circulations

In alchemy, there exist two major arms of practice: The *Circulatum majus* (Greater Circulation: Alchemy) and the *Circulatum minus* (Lesser Circulation: Spagyrics). The Greater Circulation was focused primarily on the use of minerals and metals and was fundamentally concerned with the manufacture of the *Lapis philosophorum* and other medicinal and transformative substances; whereas the Lesser Circulation was based upon the exclusive use of plants and animal products for therapeutic benefit in health. It was believed by many alchemists that the *Circulatum minus* was a precursor or primer to work in the more dangerous kingdom of minerals and metals; therefore, until mastery of this had been achieved (which was set out as producing a *lapis vegetabilis* or vegetable stone), the mineral kingdom was closed. Our modern understanding of toxicology specifically associated with minerals and metals such as antimony, lead and mercury, gives credence to this understanding, and it is well known that many naïve and ill-prepared alchemists met an untimely demise due to dabbling in the Great Work (another name for alchemy).

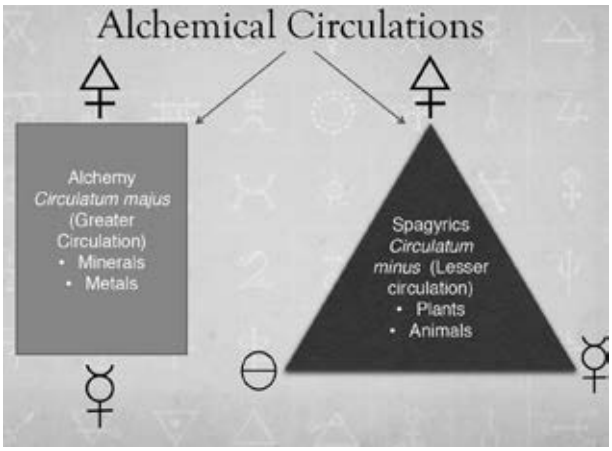

Figure 1: Diagrammatic representation of the major & minor Circulations.

Both alchemy and spagyrics relied heavily on symbolism and allegory as a way of both expressing complex procedures and philosophies and also of protecting these procedures and philosophies from those considered unworthy of the knowledge. Alchemists went to great lengths to protect this arcane wisdom, which is largely why many worked in solitude and in secret. An example of this is a postulated theory behind the

Table 1: Table of noted alchemists through history

Wei Boyang (ca.142CE)	Paracelsus (1493–1541)
Maria Prophetissa (ca.300CE)	Basilius Valentinus (ca. 15th century)
Zosimos of Panopolis (ca. 300CE)	Dr John Dee (ca. 1527–1609)
Jabir ibn Hayyan "Geber" (721–815CE)	Robert Boyle (1627–1691)
Muhammad ibn Zakariya Razi (864–930CE)	Hennig Brandt (ca. 1630–1710)
Abu Abdallah ibn Sina "Avicenna" (980–1037CE)	Sir Isaac Newton (ca. 1642–1727)
Roger Bacon (ca. 1214-1294CE)	Fulcanelli (ca. 20th century)

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etymology of the word 'gibberish' (meaning meaningless or unintelligible speech or writing) which is attributed to the alchemist Geber, and referred to the almost indecipherable technical jargon he used in concealing the Great Work in his writings.

The *Tria Prima* – the three essentials

In alchemy, the concept of the duality of opposites is a very important philosophical underpinning, and gives rise to the concept of the Two Principles. Examples of this duality include terms used in alchemical literature describing the 'Sun and the Moon' or the 'King and the Queen', and it is a similar duality that is observed in other ancient paradigms such as the symbol of the Tao (Yin / Yang) in traditional Taoist philosophy. The idea of the Two Principles was based originally upon Aristotelian concepts in trying to explain the formation of metals and their transitions from an elemental perspective (Cotnoir 2006). The Sufi alchemist Jabir ibn Hayyan (Geber) developed further upon this concept and identified that it was a matter of balancing the two forces within the metals (the sulphur and the mercury) to transmute it to its most purified and highest state (Cotnoir 2006).

Over six centuries later, Paracelsus contributed further to this idea of Geber's by stating that the 'salt', or body, was needed to be added to the Two Principle theory to bring solidity and stability. This gave birth to the *Tria Prima*, which has been the dominant thought in spagyrics since its inception and is the major differentiation between the two alchemical circulations.

The author wishes to make it very clear that whenever you see the terms "sulphur", "mercury" or "salt" in this article, it is *never* suggesting the modern chemical meaning or structure (e.g. brimstone, quicksilver or common table salt [NaCl]); it is only talking about their specific 'spagyric' or 'alchemical' meanings which are expanded upon below. These terms have both metaphysical and physical meanings that are sometimes used interchangeably and can represent a trap for the uninitiated.

The *Tria Prima* suggests that all herbal substances can be broken down into three basic components –sulphur, mercury and salt. These essentials represent both metaphysical aspects within the herb and more practical phytochemical aspects of the plant material. Please see Figure 2 below for a basic review of this information.

In modern herbal medicine, the sulphur and mercury of the plant is obtained from judicious use of a balanced menstruum to extract the 'soul' and 'spirit', however, the marc is discarded and viewed as having little therapeutic benefit. Spagyric tinctures and elixirs re-incorporate the marc back into the herbal product in the form of an ash to assist in 'fixing' the more ethereal and volatile components.

Spagyrics

The term spagyrics comes from the Greek *spao* meaning 'to tear apart' or 'draw out' and *ageiro* meaning 'to gather, to bind or to join' (Junius 1979, Cotnoir 2006). It was first coined by Paracelsus and represents the key alchemical premise of *solve et coagula* – 'separate and recombine'. This concept of separating and purifying a substance and then bringing the purified parts back into combination into a new highly energised and potentised form suggests that the alchemists did not believe that Nature was perfect, but needed assistance to raise it to a new level of exaltation.

According to a spokeswoman for the Therapeutic Goods Administration, spagyric tinctures have been included in the code tables of the Australian Register of Therapeutic Goods (ARTG) in association with herbal ingredients since July 2002 (Personal communication 2013), yet many naturopaths and herbalists are unaware of their existence as a potential herbal dosage form. This could be due to both a lack of education in this particular field of manufacturing in the tertiary academic setting, and an almost non-existent presence within the herbal marketplace. The requirement of specialist equipment, manufacturing expertise and the fact that it is a time consuming method could also be drivers for lack of interest.

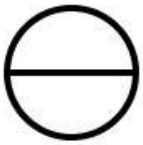
Sulphur – Soul – Masculine principle	Mercury – Spirit – Female principle	Salt – Body
		
• In spagyrics – volatile principles / oils of the plant • That which is active, formative, aggressive • Consciousness	• In spagyrics – a liquor / spirit or tincture of the plant • That which is passive, ethereal, vitalistic • Life (vital) force - Prana	• That which is solid, a vehicle, that which fixes, an alkali / salt

Figure 2: Metaphysical & physical aspects of the *Tria Prima*, taken from Junius 1979; Cotnoir 2006; Albertus 1974.

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The spagyric tincture

Qabalah and astrology feature prominently in alchemical and spagyric practice. In short, Qabalah is considered to be a system of esoteric knowledge and practices that stemmed from the Jewish tradition. Over the centuries this practice has evolved to include associations with alchemy, divination, hermeticism and other non-conventional practices that veered away from traditional Judaic philosophy. Qabalah is centred on the philosophy of the *Etz Chayyim*, or Tree of Life, which is believed to be symbolic of the spiritual evolution of man and the essence of divinity and creation. Fortune (2000) describes the Tree of Life as "*representing the cosmos in its entirety and the soul of man as related thereto*", which provides credence to the idea that the alchemical arts were not merely a materialistic pursuit, but a spiritual one also.

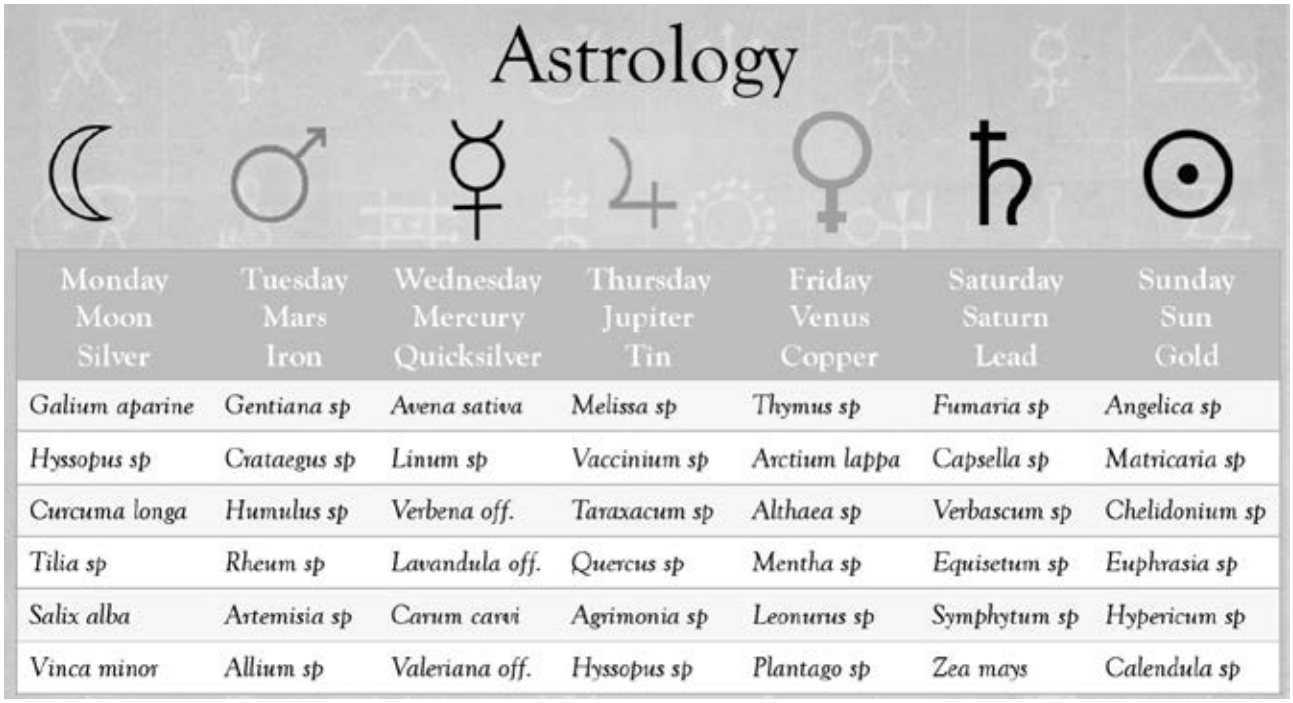
Astrology, which is defined as the study of the celestial movements and positions of the planets and stars and how they can have a "*supposed influence on events and on the behaviour of people"* (Merriam-Webster 2013) was also an important pillar on which alchemical and spagyric belief was built. Not only could this be applied to the individual being treated from a constitutional perspective, but it could also highlight specific times that are considered auspicious for manufacturing. For example, each weekday represents a ruling planet to which certain herbs or metals correspond (see Figure 3). Therefore, if a spagyric of German chamomile was desired, one would start the process of manufacturing on a Sunday. Furthermore, specific hours within the day would also be adhered to. As each 24-hour period can be broken into planetary rule, so the correct day and hour would be observed to start the specific project. Lunar cycles are also important, with waxing and waning moons causing different outcomes to the spagyric product, and new and full moons being seen as more advantageous and propitious. Such use of astrology is not unknown in herbal medicine, with noted herbalists such as Culpeper utilising this extensively in his publications.

Three major steps are required in the manufacturing of the herbal spagyric tincture, including separation, purification and cohobation.

1. Separation

Separation involves capturing the sulphur and mercury of the plant with a menstruum of water and alcohol. The alcohol used where possible should be *spiritus vini*, more commonly known as rectified spirit of wine. Alchemists believed that the ethanol obtained from grapes has a higher energetic level and contains more vital force than that derived from grains. The herb is then ground to a suitable size (comminution) with a mortar and pestle; however, machinery to reduce the herb to a smaller particle size may be needed for the tougher morphological parts of certain plants, such as the bark or roots. The appropriate menstruum for the herb is selected based on chemistry; however, many traditional alchemists such as Frater Albertus utilised a 66% ethanol to 33% (2/3:1/3) water ratio regardless of the herb being used. Other authors state that a 50:50 ratio is best (Cotnoir 2006).

The herb is then incorporated with the menstruum in a sealed glass vessel, wrapped in aluminium foil or kept in a dark place and digested for a philosophical month (40 days), being agitated several times daily. The term digestion denotes the gentle application of heat, with a temperature generally not exceeding 40°C so as to



Monday Moon Silver	Tuesday Mars Iron	Wednesday Mercury Quicksilver	Thursday Jupiter Tin	Friday Venus Copper	Saturday Saturn Lead	Sunday Sun Gold
Galium aparine	*Gentiana sp*	*Avena sativa*	*Melissa sp*	*Thymus sp*	*Fumaria sp*	*Angelica sp*
Hyssopus sp	*Crataegus sp*	*Linum sp*	*Vaccinium sp*	*Arctium lappa*	*Capsella sp*	*Matricaria sp*
Curcuma longa	*Humulus sp*	*Verbena off.*	*Taraxacum sp*	*Althaea sp*	*Verbascum sp*	*Chelidonium sp*
Tilia sp	*Rheum sp*	*Lavandula off.*	*Quercus sp*	*Mentha sp*	*Equisetum sp*	*Euphrasia sp*
Salix alba	*Artemisia sp*	*Carum carvi*	*Agrimonia sp*	*Leonurus sp*	*Symphytum sp*	*Hypericum sp*
Vinca minor	*Allium sp*	*Valeriana off.*	*Hyssopus sp*	*Plantago sp*	*Zea mays*	*Calendula sp*

Figure 3: A table of selected herbal medicines based on their ruling planets (Albertus 1974, Junius 1979, Cotnoir 2006).

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avoid damaging the heat sensitive constituents. Ancient alchemists believed it should be no hotter than was needed to hatch a chicken egg (approximately 37.5C). Digestion can take place in a gentle sand bath, which represents an excellent apparatus for low heat applications. After the appropriate duration, the tincture was strained, pressed and set aside in a sealed glass vessel, but the marc was not discarded.

2. Purification

The herbal marc is allowed to dry naturally, and then incinerated to ash in a crucible or other fire resistant vessel. This can be done in a muzzle furnace or other high temperate athanor. This is a progressive process, as once all of the herbal material has been incinerated; it will still be largely dark grey to black in colour. The ash is now transferred to a mortar and pestle and ground incredibly fine. Certain Chinese alchemical literature discusses the grinding of the alchemical material for up to 6 months, taking it to a state of impalpable fineness, which modern science can now confirm is likely to have taken the particulate matter down to a nanoparticle size (less than a micron in diameter). This process is likely to greatly increase the surface area and reactivity so that reactions are more complete and occur faster. Pharmacokinetic parameters such as absorption may also occur faster with the material having higher bioavailability within the biological system. This may be the basis as to why spagyric tinctures are considered more potent than other equivalent preparations, albeit this is only anecdotal evidence with no quantitative analytical evidence to substantiate it. Once ground finely, the ash is returned to a crucible and fired once again to higher and higher temperatures, with continued grinding in between firings as needed, until it takes on a white colour, showing the highest level of purification. All of the dross and detritus has been burned away once the white ash has been obtained, leaving the purified salts of the herb. Once this has been achieved, the salts are set aside in a glass jar.

3. Cohobation

The sulphur and mercury (tincture) is now combined with the salts (ash) in glass vessels known as 'pelicans' and allowed to cohobate. The process of cohobation, also known as circulation, is said to allow the 'elevation' and 'expansion' of the tincture, making it more powerful. The process is conducted again for a philosophical month and is digested in a sand bath. Daily agitation is not essential as the gentle application of heat 'circulates' or moves the fine particulate ash throughout the tincture. Once this process is complete, it is poured into a storage bottle and labelled, ready for use. The average dose of a spagyric tincture would be similar to other modern day tinctures based on the herb's pharmacology; however, alchemists and spagyrists consume these tinctures quite differently. The manufacture of the 'Planetary 7', that is, 7 different herbal spagyric tinctures, each coinciding with a corresponding day of the week, is a tradition which is seen as an initiatory practice of the Lesser Circulation. For example, on Monday upon rising, 5 mL of a tincture of cleavers would be consumed, followed by 5 mL of hawthorn tincture on the Tuesday, and so on in a process that would continue for an entire year. This process was thought to bring balance to the body and its various organ systems, maintaining health and vigour.

The spagyric elixir

The next level of plant mastery was the spagyric elixir. This process was seen as the next level of elevation in the vegetable kingdom, producing a more powerful and purified substance. Manufacturing the elixir involves the separation of the plant matter into its three distinct *Tria Prima*, unlike the spagyric tincture that incorporated the sulphur and mercury together (essential oil and tincture) with the inclusion of the salts.

1. Separation

Herbs of high volatile oil content are excellent for elixirs, particularly rosemary and fennel. Using fennel as an example, the whole plant (fresh, not dried) is allowed to grow until it goes to seed. The seed is then harvested and gently dried. After being bruised with a mortar and pestle, it is placed in a distillation apparatus and the oils are separated. Once all of the oils have come over in the condenser and been collected in the separating funnel, they are isolated and stored in an amber glass bottle and saved for the cohobation phase.

2. Fermentation

The fennel stalks and leaves are now cut finely and placed within a large glass (15-20 L) demi-john or fermentation vessel. Water is added along with brewing yeast (such as *Saccharomyces cerevisiae*) and a small amount of sugar to give a more stable fermentation. The vessel is sealed with an airlock and kept at a constant temperature of around 25-27°C using heating mats if required. After 24-48 hours, the fermentation process will commence and alcohol is made from the herbal material. Once the fermentation process has stopped, the mixture is distilled at 78°C (being careful to discard anything that came over before this temperature). The process is completed 7 times to produce approximately 96% pure alcohol. In spagyrics, the signature of the plant is believed to be 'imprinted' into the alcohol, which after being purified is set aside and labelled.

3. Purification

The marc from the fermentation (stalks and leaves) and the seeds from the distillation are dried and then incinerated and calcined into a fine white ash in exactly the same process as was outlined for the spagyric tincture. The three essentials (volatile oil, alcohol and salts) are then recombined in equal proportions into a glass bottle and labelled. Alternatively, this can then undergo a

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further process of cohobation if desired. Dosage of the spagyric elixir is drop dose only (literally 1-2 drops of elixir) due to the toxicity profile of the purified essential oils and should certainly not be consumed in the amounts outlined for the spagyric tincture.

The *lapis vegetabilis* (vegetable stone)

The vegetable stone represents the first historical evidence of what in modern pharmacology is known as a soft extract. The vegetable stone was perceived as the pinnacle of achievement in the *Circulatum minus* and represents one of the strongest forms of medicine in the spagyric realm. The *lapis vegetabilis* is notoriously time consuming and laborious to manufacture, with a time frame spanning from 10 – 18 months to complete, although numerous 'short-cuts' have been proposed by more modern practitioners. Traditionally, large amounts of the *Tria Prima,* generally an essential oil rich plant, are required to start this process. Certain amounts of all three essentials are placed into a specialised flask which is then hermetically sealed and deposited in a sand bath at 40°C. As the salts (purified ash) take up the sulphur and mercury (essential oil and alcohol) it starts to congeal and thicken, at which time more sulphur and mercury may be added in small amounts. This process of 'feeding' the stone can take months until eventually it cannot take anymore in and the process has been completed.

Conclusion

Herbal medicine, as well as modern sciences like chemistry, can claim a direct lineage to alchemical and spagyric practices. Whilst no direct scientific evidence exists within the literature regarding spagyric tinctures, elixirs or the vegetable stone, this should not necessarily discount their relevance as a traditional dosage form.

The author would strongly advise caution before attempting the manufacture of any of these dosage forms without first seeking appropriate training in the requisite use of laboratory glassware, spagyric manufacturing methods and safety in handling of the various chemicals and solvents. State and federal laws for owning such glassware, chemicals and stills are also in effect nationwide and should be respected. A recommended reading list has been included for those who wish to learn more about these dosage forms.

In finishing, of particular relevance in this paper was the alchemical concept of the duality of opposites, a topic quite pertinent in the herbal and naturopathic profession at present. This duality represents a philosophical one as our profession continues to evolve its expanding evidence base, and a schism appears to be growing between our more traditionally trained practitioners and those that embrace a more modern and scientific approach.

The profession is currently going through its own transmutation of sorts, our own evolutionary change, and the question that remains to be answered is what will come of it? Tradition and science are not chalk and cheese, but rather simply represent differing ends of the same spectrum we call 'evidence'. You cannot have one without the other. Each one drives the other, enriches the other, teaches the other and even supports the other. Science is knowledge, but tradition represents wisdom – both important attributes in either practitioner or paradigm. The profession cannot forget or disregard our traditional evidence or we may risk losing our own identify in a near frenzied push for acceptance by a modern medical model that developed out of our own tradition. Conversely, we cannot cling to certain traditional beliefs that have been proven incorrect by science.

Based on our evidence, what does it mean to be a herbalist or naturopath in this day and age? How far removed are we from our traditional roots? How much tradition should we cling to? Should scientific advances in herbal medicine theory and usage supersede our traditional evidence on a hierarchical scale of importance for us as practitioners, or for the teaching of current students, who are our profession of the future?

Whilst our continued growth and evolution as a profession is assured, it is now time to set in motion this discussion so we may thoughtfully and diligently consider the importance of where we have come from, and where we are going…

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Anti-inflammatory activity of the leaves of *Bergia suffruticosa* investigated on acute and chronic inflammation models in rats

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Abstract: *Bergia suffruticosa* (Delile) Fenzl (Syn. *B. odorata* Edgew) (Elatinaceae) is used ethnomedically to repair bones and heal wounds. The anti-inflammatory activity of the hydro-methanolic extract of the leaves of *Bergia suffruticosa*, and fractions of that hydro-methanolic extract, were studied in acute and chronic models of inflammation in Sprauge-Dawley rats. Hydro-methanolic extract, *n*-hexane fraction, ethyl acetate fraction, *n*-butanol fraction, aqueous fraction, positive controls (anti-inflammatory drugs: ibuprofen and etoricoxib for acute and chronic study, respectively), each suspended in 0.2% agar, were administered orally to the seven groups of rats (6 animals/group). The vehicle control group received only 0.2% agar. Carrageenan (1%) was used as a pro-inflammatory agent in the acute study whereas formalin (2%) was used for inducing chronic inflammation in the right hind paw of rats. The reduction of inflammation in the acute study was in the range of 71-92% and 71-85% for *n*-hexane and ethyl acetate fractions, respectively. In the chronic study, reduction in oedema ranged between 81-86% for *n*-hexane and 75-81% for ethyl acetate fraction. The anti-inflammatory activity of *n*-hexane fraction of *Bergia suffruticosa* was comparable with the positive controls.

Keywords: Carrageenan, formalin, lupeol, β-sitosterol, gallic acid, gallicin.

Introduction

Inflammation, in its broadest sense, is a host response to tissue injury. The four ancient cardinal signs of inflammation are rubor (redness), calor (heat), tumor (swelling) and dolor (pain). These clinical signs of inflammation are, of course, the macroscopic culmination of molecular and cellular processes, many of which have become well defined over the last 120 years and many of which may be reproduced in convenient experimental systems both *in vitro* as well as *in vivo* (Winyard 2003). The inflammatory cascade is associated with many diseases *viz.* rheumatoid (arthritis), respiratory (asthma), cutaneous (psoriasis) and inflammatory bowel disorder (Franklin 2008). However treatment of these disorders becomes difficult due to multifactorial and multigenic involvement of several proteins in the disease cascade. The current clinical therapeutic regimens include non-steroidal anti-inflammatory drugs (NSAIDs), cycloxygenase-2 (COX-2) inhibitors, disease-modifying anti-rheumatic drugs (DMARDs) and corticosteroids (Willough 2000, Felson 1992). Since the isolation of salicin from *Salix alba*, herbal sources have also been relied upon for identifying some potential candidates for the management of inflammatory disorders.

Bergia suffruticosa (Delile) Fenzl (Syn. *B. odorata* Edgew) (Elatinaceae) is used traditionally to repair bones and heal wounds (Kirtikar 1991). Ethnomedical studies also report its use in gastro-intestinal disorders (Yousif 1983) and as an antidote to scorpion stings (Bedi 1978). The plant is reported to show antibacterial activity against *Bacillus subtilis*, *Escherichia coli*, *Staphylococcus aureus* and *Pseudomonas aeruginosa* (Farouk 1983). The 95% ethanol extract of the whole plant is reported to exhibit molluscicidal activity against *Bomphalaria pfeifferi* and *Bulinus truncatus* (Ahmed 1984). A phytochemical study has reported the presence of gallic acid (Figure 1a.), gallicin (Figure 1b.), lupeol (Figure 1c.) and β-sitosterol (Figure 1d.) in the plant (Anandjiwala 2007a). These compounds are reported for showing anti-inflammatory activity (Kroes 1992, Kim 2006, Delporte 2005, Geetha 2001). Another report stated that the methanolic extract of *B. suffruticosa* exhibits good free-radical scavenging activity (Anandjiwala 2007b). Based on these reports, *in vivo* anti-inflammatory activity of the hydro-methanolic extract of *B. suffruticosa* and its four solvent fractions were evaluated against carrageenan-induced acute inflammation and formalin-induced chronic inflammation in rats.

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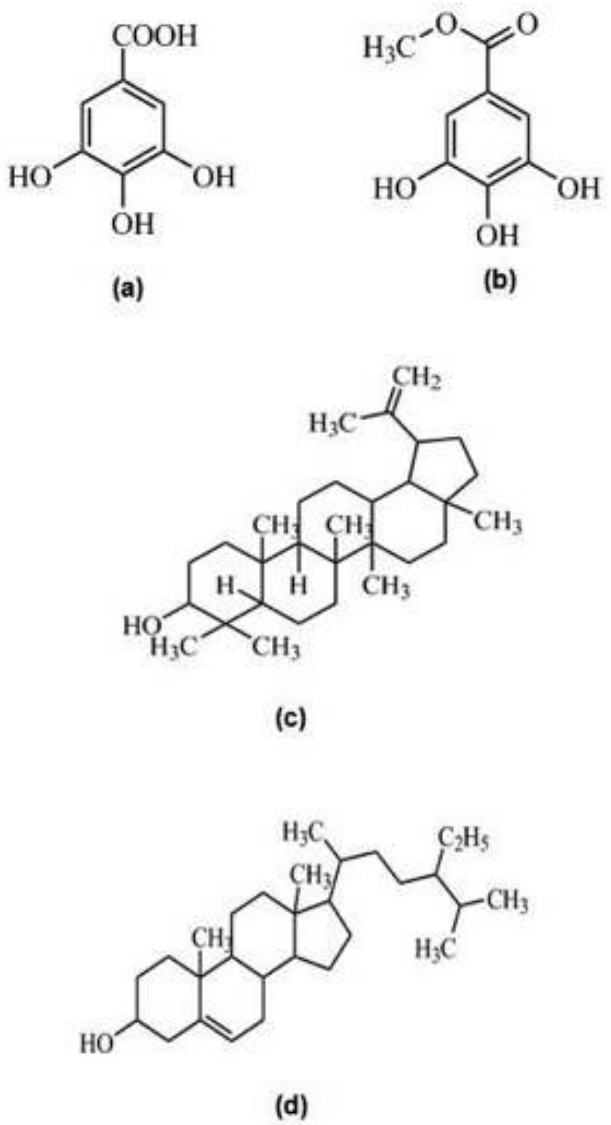

Figure 1: Chemical structures of (a) Gallic acid (b) Gallicin (c) Lupeol (d) β-sitosterol.

Experimental

Drugs and chemicals

Carrageenan was purchased from Spectrochem, Mumbai, India and formalin from Rankem, New Delhi, India. Ibuprofen was purchased from Abbott India Ltd., India and etoricoxib from Unichem Laboratories, India. Agar was purchased from Qualigen Fine Chemicals, Mumbai, India. Gallicin was purchased from ICN Biomedicals, California, USA. Gallic acid was a gift sample from Tetrahedron, Chennai, India. Lupeol was obtained as a gift sample from SC Pal College of Pharmacy, Nasik, India and β-sitosterol was purchased from Natural Remedies, Bengaluru, India. Anisaldehyde was purchased from SD Fine Chemicals, Mumbai, India. All the solvents used were of analytical grade. Deionized water used for extraction was prepared in-house using a water purifier system (Millipore Elix, Germany).

Animals

Healthy, Sprague-Dawley albino rats 12-16 weeks old of either sex (200-250 g) were obtained from the animal house of the BV Patel Pharmaceutical Education and Research Development (PERD) Centre, Ahmedabad. Animal housing and handling were performed according to Committee for the Purpose of Control and Supervision of Experiments on Animals (CPCSEA) guidelines. The animals were housed singly per cage in polypropylene cages and placed in the experimental room where they were allowed to acclimatize for a week before experiment. A 10% exhaust air conditioning unit was used to maintain a relative humidity of 60 ± 5% and a temperature of 25 ± 3°C in the animal house facility. A 10:14 h light:dark cycle was also regulated for the experimental animals. Amrut-certified rodent diet (Maharashtra Chakan Oil Mill) and tap water (boiled water cooled to room temperature) was provided *ad libitum* to the experimental animals. All experimental protocols were reviewed and accepted by the Institutional Animal Ethics Committee (IAEC) prior to initiation of the experiment.

Plant material and preparation of the extract and its solvent fractions

Leaves of *B. suffruticosa* were collected from the botanical garden of the PERD Centre in the month of February, 2010 and authenticated by Dr Sheetal Anandjiwala (taxonomist). A specimen of the collected plant was preserved in the Department of Pharmacognosy and Phytochemistry at the PERD Centre (Herbarium Specimen #: BVP/PP/17/02/10). The leaves were washed, shade-dried, stored in an airtight container and powdered to 40 mesh as and when required. Initially, dried powdered leaves (500 g) were extracted with 50% methanol under reflux on a water bath at 50°C. The hydro-methanolic extract (HME) obtained was cooled, filtered and then concentrated under vacuum at 40°C. The yield of HME was 38 g (7.60%). This extract was then re-suspended in deionised water and partitioned successively in a separating funnel using organic solvents of increasing polarity *viz*. *n*-hexane (250 ml × 3), ethyl acetate (250 ml × 3) and *n*-butanol (250 ml × 3). Solvents were evaporated under vacuum to obtain fraction of *n*-hexane (316 mg), ethyl acetate (3.80 g), *n*-butanol (3.57 g) and aqueous or remnant (17.09 g) respectively. Fractions were stored in the refrigerator at 4°C until further use.

TLC fingerprint profile of n-hexane and ethyl acetate fraction of B. suffruticosa

Our previous report on *B. suffruticosa* showed the presence of β-sitosterol, lupeol, gallic acid and gallicin in hydro-methanolic extract of *B. suffruticosa*. Thus, in continuation from the previous study, fractionation of the hydro-methanolic extract was carried out and fractions containing these compounds were determined. The *n*-hexane and ethyl acetate fractions (100 mg each) of *B.*

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suffruticosa leaves were dissolved in 50 ml of *n*-hexane and ethyl acetate respectively and used for the TLC (thin layer chromatography) fingerprinting profile. TLC plates used were of 10 × 10 cm, precoated with silica gel 60 F_{254} TLC plates (Merck, Darmstadt, Gemany) (0.2 mm thickness) with aluminum sheet support. The spotting device consisted of CAMAG Linomat V Automatic Sample Spotter (Camag Muttenz, Switzerland) and a syringe, 100 µL (Hamilton, Switzerland). The plates were developed in a CAMAG glass twin trough developing chamber (10 × 10 cm) at a temperature of 25 ± 2°C and relative humidity of 40%. Preliminary TLC experiments were done in order to determine the presence of gallic acid and gallicin in the ethyl acetate fraction and β-sitosterol and lupeol in the *n*-hexane fraction. TLC fingerprint of the *n*-hexane fraction (2 mg/ml) was developed along with the standards of β-sitosterol and lupeol using the solvent system toluene:methanol (9:1 *v:v*). The plate was then derivatised with anisaldehyde-sulfuric acid reagent which was prepared according to the method described by Wagner *et al.* Briefly, 0.5 ml of anisaldehyde was added to 10 ml of glacial acetic acid. To the above solution, 85 ml of methanol and 5 ml of concentrated sulphuric acid were added to obtain anisaldehyde-sulfuric acid reagent. After spraying of the derivatising agent, the plate was heated at 100°C until the coloured band become visible in white light. Similarly, TLC fingerprint for the ethyl acetate fraction (2mg/ml) along with the standards of gallic acid and gallicin was developed in the solvent system toluene:ethyl acetate:methanol:formic acid (12:6:2:1 *v:v:v:v*). The plate was observed under UV 254 nm.

Carrageenan-induced paw oedema in rats: acute inflammation

Seven groups (6 rats per group) of either sex were used for the study. The paw oedema was induced in rats by injecting 0.1 ml of 1% carrageenan (a pro-inflammatory agent; prepared in normal saline) subcutaneously in the sub-plantar region of right hind paw, 1 h after administration of the test drugs. The preliminary evaluation started with the determination of anti-inflammatory activity of hydro-methanolic extract at a dose of 500 mg/kg bodyweight, given orally. The determination of the dose of the extract for this study was based on one of our previous studies (Thakura 2013). The findings of our previous study confirmed that these extracts are not ulcerogenic, which is a predominant adverse effect of most of the anti-inflammatory drugs. The extract was then further fractionated with *n*-hexane, ethyl acetate, *n*-butanol and water. The doses of the fractions were determined according to their extractive values with reference to the hydro-methanolic extract. The doses for individual fractions were: *n*-hexane fraction, 4.16 mg/kg of bodyweight; ethyl acetate fraction, 50 mg/kg bodyweight; *n*-butanol fraction, 46.95 mg/kg bodyweight; aqueous fraction, 224.82 mg/kg of bodyweight. Ibuprofen (dose: 100 mg/kg of bodyweight) was taken as positive control for the acute inflammation study. All the test drugs were administered orally as a suspension in 0.2% agar and the animals in the vehicle control group received 0.2% agar only.

The paw volumes of rats were measured using digital plethysmometer (IITC Life Science, California, USA), before and after injection of 1% carrageenan at different time intervals (1, 2, 3, 4, 5, 6, 8, 12 and 24 h). Changes in paw volume, in millilitres (ml) of water displaced, were recorded at above time intervals with reference to the initial volume before administration of the inflammatory agent.

Formalin-induced paw oedema in rats: chronic inflammation

Seven groups (6 rats per group) of either sex were used. In the chronic study, inflammation in the right hind paw of the animals were induced by injecting 0.1 ml of 2% formalin (prepared in normal saline) subcutaneously in the sub-plantar region of right hind paw, 1 h after administration of the test substances and etoricoxib (anti-inflammatory drug as positive control) for five consecutive days. The dose of etoricoxib was 10 mg/kg bodyweight. The changes in paw volume were recorded using the digital plethysmometer before and after injection of 2% formalin at different time intervals (1, 2, 3, 4, 5, 6, 8, 12 and 16 h).

Statistical analysis

One-way ANOVA followed by Dunnett's multiple comparison test was applied to determine the significance of any difference in anti-inflammatory activity of different fractions of *B. suffruticosa*. Probability values with $p \leq 0.05$ were considered to be significant. Anti-inflammatory activity of positive control and different solvent fractions were compared with the vehicle control group.

Results and Discussion

TLC fingerprint profile

TLC fingerprint profile of *n*-hexane fraction of *B. suffruticosa* showed the presence of β-sitosterol and lupeol (Figure 2). The colours of the band of β-sitosterol and lupeol were violet and light purple respectively after derivatisation with anisaldehyde-sulphuric acid reagent. Similarly, the presence of gallic acid and gallicin was confirmed from the TLC fingerprint profile of ethyl acetate fraction (Figure 3). TLC fingerprinting could not be done for butanol and aqueous fraction because loading/spotting would have been difficult and might not show good resolution on TLC plates. Moreover, butanol and aqueous fractions were also not found to be very pharmacologically effective.

Anti-inflammatory activity of the hydro-methanolic extract and its solvent fractions

The anti-inflammatory effects of the hydro-methanolic

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extract (dried leaves of *B. suffruticosa*) and its four solvent fractions on carrageenan-induced acute inflammation was measured by the changes in paw volume (ml of water displaced) of the rats at different time periods (1, 2, 3, 4, 5, 6, 8, 12 and 24 h) as presented in Table 1. The paw volume in the vehicle control group (0.2% agar) increased up to 4 h and thereafter declined slowly (at 24 h: 0.50 ml). Pre-treatment with the anti-inflammatory drug (ibuprofen) significantly reduced the oedema (~67% reduction) at 1 h, and at 24 h around 95% reduction in oedema was observed ($p \leq 0.05$). The hydro-methanolic extract showed some anti-inflammatory activity with the reduction in oedema between 52-71%, but this was not statistically significant. The two solvent fraction groups, *n*-hexane and ethyl acetate, showed similar, significant reductions ($p \leq 0.05$) in oedema to those shown by the positive control group. The reduction for the *n*-hexane fraction (71-92%) was higher compared to reduction observed for ethyl acetate fraction (71-85%). However *n*-butanol and aqueous fractions did not show good anti-inflammatory activity (data not represented).

Table 2 shows chronic anti-inflammatory effects of the hydro-methanolic extract and its solvent fractions along with etoricoxib, in formalin-induced paw oedema in rats at 16 h. The anti-inflammatory activity was determined in terms of change in paw volume. Etoricoxib reduced the formalin induced oedema by 81-88% in five days ($p \leq 0.05$). The hydro-methanolic extract reduced the paw volume by 50-56%, but this was not statistically significant. However the *n*-hexane and ethyl acetate fractions showed good chronic anti-inflammatory effects which were comparable to etoricoxib. The *n*-hexane fraction reduced the paw volume by 81-86%, and the ethyl acetate fraction by around 75-81%, whereas the *n*-butanol and aqueous fractions did not show any significant reduction in inflammation (data not presented). A significant difference was observed in the anti-inflammatory effect of the *n*-hexane and ethyl acetate fractions when compared to the animals treated with agar (0.2%) only, with $p \leq 0.05$, though no significant difference was found between the groups treated with *n*-hexane, ethyl acetate and positive controls.

The results of this study indicated that the *n*-hexane and ethyl acetate fractions of the hydro-methanolic extract of the leaves of *B. suffruticosa* showed significant activity in acute and chronic inflammation models. Metabolism of

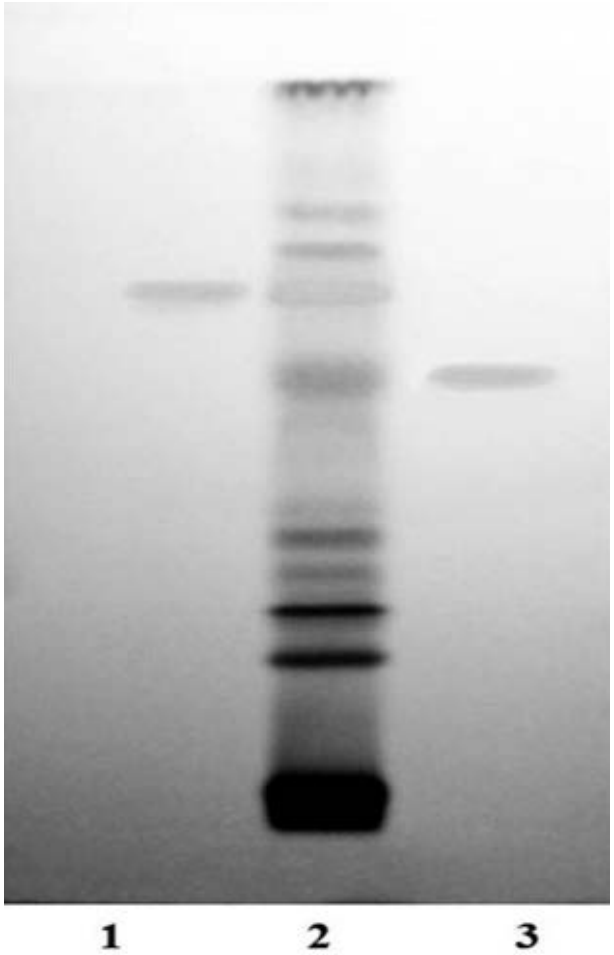

Figure 2: TLC fingerprint profile of n-hexane fraction of hydro-methanolic extract of *Bergia suffruticosa* leaves.
1 lupeol standard; 2 sample solution; 3 β-sitosterol standard.

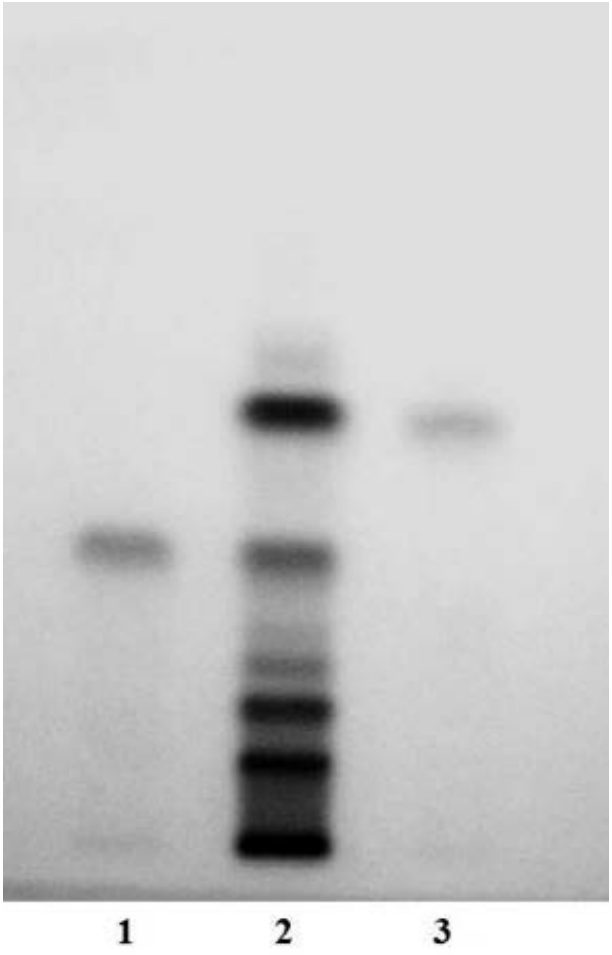

Figure 3: TLC fingerprint profile of ethyl acetate fraction of hydro-methanolic extract of *Bergia suffruticosa* leaves.
1 gallic acid standard; 2 sample solution; 3 gallicin standard.

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Table 1: Anti-inflammatory effects of hydro-methanolic extract and the solvent fractions of *Bergia suffruticosa* on carrageenan-induced acute inflammation

Treatment (mg/kg of body weight)	Time intervals (h)								
	1	2	3	4	5	6	8	12	24
Agar (0.2 %)	0.30±0.08	0.50±0.08	0.78±0.13	1.18±0.13	1.08±0.13	1.03±0.15	0.95±0.17	0.75±0.13	0.50±0.08
IBF (20)	0.10±0.08	0.23±0.09	0.38±0.13	0.30±0.08	0.25±0.17	0.23±0.13	0.20±0.16	0.15±0.13	0.03±0.05
%	67	55	52	75	77	78	79	80	95
HME (500)	0.10±0.02	0.20±0.03	0.38±0.15	0.45±0.10	0.40±0.08	0.35±0.13	0.28±0.15	0.23±0.09	0.20±0.12
%	67	60	52	62	63	66	71	70	60
HF (4.16)*	0.03±0.05	0.10±0.08	0.23±0.09	0.30±0.08	0.28±0.09	0.23±0.05	0.20±0.08	0.15±0.13	0.08±0.05
%	92	80	71	75	74	78	79	80	85
EAF (50)*	0.05±0.06	0.13±0.15	0.23±0.26	0.34±0.21	0.30±0.29	0.28±0.26	0.18±0.21	0.13±0.15	0.08±0.09
%	83	75	71	72	74	73	82	83	85

Values expressed in millilitres of water displaced in the plethysmometer as mean ± standard deviation computed over six animals/group.

Percentages refer to the change in edema size relative to the Agar (0.2%) vehicle control group.

Agar (0.2%): vehicle control, IBF: ibuprofen, HME: hydro-methanolic extract, HF: hexane fraction, EAF: ethyl acetate fraction.

*$p \leq 0.05$ as compared to vehicle control group.

Table 2: Anti-inflammatory effects of hydro-methanolic extract and the solvent fractions of *Bergia suffruticosa* on formalin-induced chronic inflammation

Treatment (mg/kg of body weight)	Change in Paw volume (% reduction in paw volume)				
	Day 1	Day 2	Day 3	Day 4	Day 5
Agar (0.2 %)	0.40±0.12	0.40±0.12	0.40±0.12	0.40±0.12	0.35±0.10
ETX (10)	0.08±0.08	0.08±0.05	0.06±0.02	0.06±0.02	0.06±0.02
%	81	81	88	88	88
HME (500)	0.18±0.05	0.18±0.05	0.18±0.05	0.18±0.05	0.17±0.05
%	56	56	56	56	50
HF (4.16)*	0.08±0.05	0.08±0.05	0.08±0.05	0.08±0.05	0.05±0.02
%	81	81	81	81	86
EAF (50)*	0.10±0.08	0.10±0.08	0.08±0.05	0.07±0.03	0.08±0.02
%	75	75	81	80	81

Values expressed in millilitres of water displaced in the plethysmometer as mean ± standard deviation computed over six animals/group.

Percentages refer to the change in edema size relative to the Agar (0.2 %) vehicle control group.

Agar (0.2%) — vehicle control to ETX: etoricoxib, HME: hydro-methanolic extract, HF: hexane fraction, EAF: ethyl acetate fraction.

*$p \leq 0.05$ as compared to vehicle control group.

arachidonic acid via cyclo-oxygenase and lipooxygenase enzyme pathways results in acute inflammation (Moura 2005). Acute inflammation has two phases: the first phase (begins immediately after injection and lasts for about 1 h) is characterized by the release of histamine and serotonin; and the second phase (beginning after about 1 h) is characterized by the bradykinin release via prostaglandin mediator pathways (Garcia-Pastor 1999). As both *n*-hexane and ethyl acetate fractions significantly offered protection against inflammation at 1 h and reduced the paw volume to near normal level by 24 h, it can be concluded that they are effective in both the phases, similarly to ibuprofen.

Chronic inflammation occurs due to fibroblast proliferation and this subsequently results in the formation of granulomatous tissues. At this stage, the body fails to respond to anti-inflammatory agents (Gepdiremen 2004). However the results of this study concluded that *n*-hexane (~79%) and ethyl acetate fraction (~82%) showed potent chronic anti-inflammatory activity which was comparable to etoricoxib (85%). The inflammatory process is reported to be associated with the generation of reactive oxygen

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species (Jung 2005). The anti-inflammatory activity of these fractions may be attributed to their free-radical scavenging activity due to the presence of the flavonoids gallic acid, gallicin, β-sitosterol and lupeol. Flavonoids are known for their potent anti-oxidant and anti-inflammatory activities by inhibiting the cyclooxygenase and lipooxygenase pathways of arachidonate metabolism (Pelzer 1998, Zheng 2003). Gallic acid, gallicin, β-sitosterol and lupeol are also reported for anti-inflammatory activity (Kroes 1992, Kim 2006, Delporte 2005, Geetha 2001). However the TLC fingerprint profile of *n*-hexane and ethyl acetate fractions of *B. suffruticosa* showed the presence of many other compounds which may also contribute to this anti-inflammatory activity.

In order to address the toxicological aspect of this study, haematological analysis, serum biochemical analysis and histological evaluation of liver, spleen and kidney of all the animals used in the experiment was carried out, after the termination of the study. The results obtained did not show any abnormalities in any of the animals and hence the data is not presented.

Conclusion

The current findings demonstrate for the first time that *B. suffruticosa* extract and its fractions (*n*-hexane and ethyl acetate fraction) show significant anti-inflammatory activity. The pharmacological mechanism(s) that might account for the effects of *B. suffruticosa* are yet to be determined. Further investigations are required to isolate the active constituents responsible for these activities and assess the generality of the current findings.

Conflict of interest

The authors declare that there are no conflicts of interest.

Acknowledgement

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Herbal treatment for hepatotoxicity associated with high fat diet, methamphetamine use and anxiety: a case study

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Abstract: A 41-year old male presented with complaints of anxiety, fatigue, hyperlipidaemia and hypercholesterolaemia, and lowered libido associated with regular methamphetamine abuse. He had been using diazepam (5mg) *ad hoc* for treatment of his anxiety and also abdominal injections of human growth hormone (1 IU/day) for gym training. The patient requested a herbal prescription for lipid and cholesterol dysfunction and also a 'natural testosterone' increasing supplement for his gym training. A herbal formulation was prescribed consisting of hydroethanolic extracts of schisandra (*Schisandra chinensis*), rosemary (*Rosmarinus officinalis*) and turmeric (*Curcuma longa*), with *Silybum marianum* provided in tablet form. In addition, SAMe was prescribed as an additional mechanism against oxidative stress.

In a follow up visit 1 month later, the patient's blood lipid and cholesterol parameters had normalised, and a hydroethanolic extract of tribulus (*Tribulus terrestris*) was prescribed. Further, the patient was advised to consume a low fat, sulphur rich diet and green tea to assist in increasing endogenous and exogenous forms of antioxidants that may reduce harmful effects of a high fat diet and also methamphetamine use.

Introduction

Amphetamines remain one of the most commonly used illicit drugs in Australia (Australian Crime Commission 2012). Amphetamines (Figure 1) have toxic effects on several body organs (Alberta Health Services 2010) and use is associated with a reduction in restful sleep (Comer 2001), increased paranoid behaviour, aggression and hepatotoxicity (Jones 1994). Further biochemical changes include hepatic adenosine triphosphate (ATP) and glutathione (GSH) depletion as evidenced in isolated hepatocytes (Beitia 1999), and modulation of transaminase enzymes of the liver, in particular elevation of aspartate transaminase (AST) and alanine aminotransferase (ALT) levels (Jones 1994). This case study reports methamphetamine abuse which presented with anxiety and hepatotoxicity. Poor diet choices also appeared to exacerbate the liver disease.

Presenting complaint

A 41-year old Australian male presented with complaints of general anxiety with panic attacks. He had periodically disturbed sleep (once to twice per week) and suffered from periods of fatigue. He also suffered with minor paralysis of the left arm periodically and was voluntarily attempting to withdraw from weekly methamphetamine use.

Past medical history

The patient was using diazepam (5mg) *ad hoc* to treat the symptoms of anxiety, i.e. panic attacks. He also used abdominal injection of prescribed human growth hormone (HGH) (somatotrophin) (1 IU/day) to supplement his gym training. The patient wanted to increase gym training but testosterone therapy was contraindicated due to excessively high cholesterol and liver damage (advice received from the general practitioner prescribing his

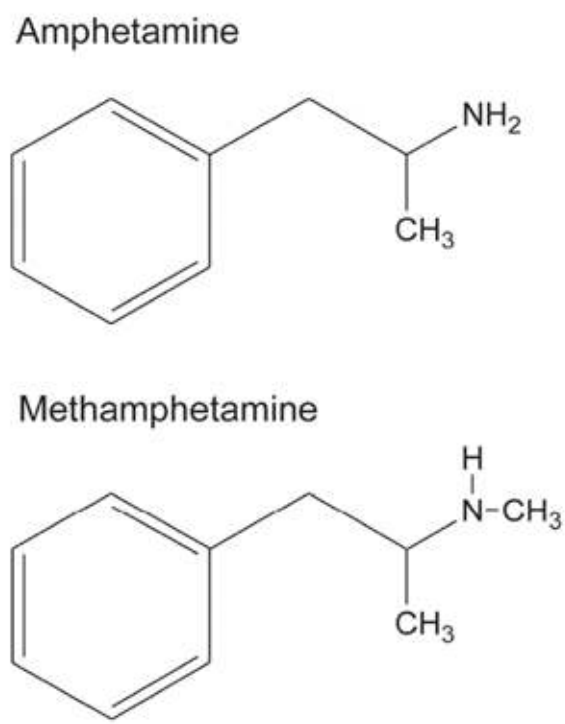

Figure 1: Chemical Structure of Amphetamine and Methamphetamine.

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somatotrophin). The patient also presented with a history of untreated hypercholesterolaemia, hyperlipidaemia and hypertension due to a poor diet and hepatic dysfunction associated with high alcohol intake (Medici *et. al.* 2011) and reduced hepatic SAMe concentration in methamphetamine addiction (Cooney *et. al.* 1998).

Social/family history

The patient smoked methamphetamines for recreational use (10 years) using a glass pipe. The quantity varied and the patient could not recall the amount consumed regularly, but did state that he smoked it occasionally or once a week depending on meeting his social acquaintances. He occasionally consumed one methylenedioxymethamphetamine (MDMA) tablet at social events (monthly). The patient was a social drinker and tobacco smoker but, in an attempt to replace methamphetamine use, he would often binge drink red wine or beer. Otherwise, he only drank 2 glasses of red wine per week. He was financially independent and undertook gym training 5 days/week which included bike riding of 40 km/week. Approximately 50% of the time he ate self-cooked food at home, but also enjoyed eating out of the home, particularly fattier meals after training. The patient was not in an active relationship and also complained of loss of libido.

Physical examination

Normal anthropometric measurements, though the patient was 'heavy' for his height. He had low body fat and high muscle mass (reflective of his gym program), except for the abdominal region. Eyes appeared tired and sore. Body weight: 88.50kg; height: 164cm; body mass index (BMI): 32.85 kg/m^2; waist: 103cm, hip: 103cm; waist to hip ratio (W:H): 1.0; pulse: 84 beats per minute (bpm); blood pressure (BP): 141/62 mmHg. Cardiovascular and respiratory systems were normal, as confirmed by a previous consultation with a medical general practitioner.

Biochemical investigations

Free testosterone and high density lipoprotein cholesterol (HDLC) were low (8 pg/mL and 12 mmol/L respectively), whereas his plasma aminotransferase/ alanine aminotransferase (AST/ALT), and triglycerides levels were very high (135 IU/L, 85 IU/L and 5 mmol/L respectively). His LDL: HDL ratio was 24:1.

Diagnosis

Chronic anxiety, acute panic attacks, lipid and cholesterol dysfunction in addition to loss of libido due to methamphetamine use.

Herbal treatment

The patient was advised to stop amphetamine use with a dietary modification (i.e. low fat diet). A combination of herbal prescription in addition to dietary evaluation and modification was suggested. Herbal medications included St Mary's thistle (*Silybum marianum*) standardized extract 'Silymarin' (Mediherb, Warwick, Queensland, Australia), 400 mg/day; and SAMe (s-adenosyl methionine) (Nutrition Care Pharmaceuticals, Keysborough, Vic, Australia), 400 mg/ day for liver dysfunction (i.e. steatosis, inflammation, fibrosis, alteration in ALT and AST). Further, the very low testosterone, very low HDLD and elevated low-density lipoprotein cholesterol (LDLC) were addressed by treating liver dysfunction further using a '*Liver Detoxification Formula*' (Table 1). After 1 month of treatment and normalisation of cholesterol ratio (LDL: HDL) and liver damage parameters, the patient was prescribed a standardised 40% ethanol extract of a 1:2 extract ratio of tribulus (*Tribulus terrestris*) (Mediherb, Warwick Queensland, Australia) 4 mL/day for low libido/ sexual dysfunction.

Treatment rationale

Silybum marianum (compressed tablet) was prescribed as the patient displayed physiological signs of liver damage as evidenced by increased plasma ALT and AST enzymes in plasma. *S. marianum* has been evidenced to reduce ALT and AST in patients with non-alcoholic fatty liver disease (Cacciapuoti 2013). *S. chinensis,* a herb often used for liver damage, has been shown to reduce ALT and AST levels in vivo (Cheng 2013). Both the aqueous extract (AQ) and non-esterified phenolic fraction (NEPF) from *R. officinalis* have been shown to have high anti-oxidant capacity due to increased activity of superoxide dismutase (SOD), catalase (CAT) and glutathione peroxidase (GPX) in vivo (Afonso 2013). *R. officinalis* may also be beneficial for hypercholesterolaemia (Ibarra et al 2011). *C. longa* has been shown to ameliorate hyperlipidaemia in high fat fed hamsters (Singh 2013), as well as possess hepatoprotective effects (fermented turmeric powder; FTP, 3g/d/12 weeks), especially to

Table 1: Liver detoxification formula*

Common name	Botanical name	Extract ratio	Amount
Schisandra	*Schisandra chinensis*	1:2	33 mL
Rosemary	*Rosmarinus officinalis*	1:2	34mL
Turmeric	*Curcuma longa*	1:2	33mL

* Dose: 5mL twice daily with 100-150ml of warm water or juice. Hydroethanol extracts were obtained from Mediherb, Warwick Queensland, Australia).

Additionally, St Mary's thistle seed (*Silybum marianum*), (tablet dried extract) was added (400 mg/d).

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reduce elevated alanine transaminase (ALT) levels in patients, as shown in a randomised, double-blind, placebo-controlled trial (Kim 2013).

SAMe is a dietary precursor of cysteine and a component of glutathione, a major physiologic defence mechanism against oxidative stress. Additionally, SAMe synthetase is an enzyme decreased in liver disease (Lieber 2002) and in the liver of methamphetamine users (Cooney 1998). Accordingly, dietary supplementation is essential when SAMe production is limited by these factors as reduced enzyme levels may cause depletion. As SAMe is the chief methyl donor used by dopamine in neurotransmitter metabolism in mammals, reduced levels may lead to depression.

Further, the steroidal saponin (protodioscin and protogracillin) as a hydroethanolic 1:2 liquid extract of *Tribulus terrestris* was prescribed after 1 month when hypercholesterolaemia ceased. Hydroethanolic extracts of *Tribulus alatus* have been shown in male rats to increase free serum testosterone (El-Tantawy 2007), though studies in humans conclude that supplementation with *T. terrestris* supplementation does not increase free testosterone precursor androstenedione (Brown 2000). *T. terrestris* has been shown to improve libido in vivo (Gauthaman 2002), but human trials are lacking.

Dietary instructions

The patient was further advised to reduce fat intake and eat more sulphur-containing vegetables such as broccoli which contain the anti-oxidant sulforaphane which stimulates endogenous GSH production and reduces neurotoxicity associated with methamphetamine intake (Chen 2012). The patient was also advised to consume raw green tea powder processed in a fruit/vegetable smoothie due to its lipolytic effect (Cichello 2013).

Follow up

1 month: The patient's general wellbeing had improved and he felt more healthy and confident. He continued a low fat diet and also self-elected to pursue a whole food and mostly vegetarian diet utilising soy or whey protein supplements. Pulse rate: 75 bpm, BP: 135/65 mmHg, weight 85kg; height: 164cm, BMI: 31.6 kg/m^2; waist: 96cm; hip: 99cm, W:H ratio: 0.97. With the cessation of amphetamine use and improvements in diet, the patient did not complain of ongoing panic attacks.

4 months: General wellbeing improved further and the patient continued on the diet as advised. On examination: pulse rate: 71 bpm, BP: 130/63mmHg, weight 78kg, height: 164cm, BMI: 29.0 kg/m^2, waist: 91cm, hip: 99cm, W:H ratio: 0.92. Biochemical investigations confirmed normalisation of testosterone (20 pg/L) and AST/ ALT enzymes (<35 IU/L).

Discussion

Methamphetamine use is associated with a myriad of health effects including a reduction in restful sleep (Comer 2001), hepatotoxicity (Jones 1994), modulation of AST and ALT hepatic transaminase enzymes (Jones 1994) with associated hyperlipidaemia and hypercholesterolaemia. The causes of hyperlipidaemia and hypercholesterolaemia in this case were most likely of dietary origin as this patient did not present with a history of hyperthermia induced hepatotoxicity caused by amphetamine use. A dietary regime of reduced processed foods and animal fats with increased fruit and vegetable intake, whey and in particular soy-based proteins have been shown to be beneficial for hypercholesterolaemia (Maki 2010), as has raw green tea intake at 2% of diet (Cichello 2013). The patient's mental health was also significantly improved as a result of stopping the methamphetamine use.

Conclusion

Long term use of amphetamines (10 years) had perhaps resulted in several of the patient's problems, with disruption to his professional and personal life which had worsened his physical, psychological and social wellbeing.

The treatment was provided to reduce liver damage, improve lipid parameters, increase libido and improve sleep. In addition, lifestyle measures, dietary improvement of less refined foods and lower fat and cholesterol intake also helped to improve his condition.

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The
Herbal Extract
Company of Australia

MARITIME PINE
Pinus pinaster
bark
1:1
200mL

MARITIME PINE
Pinus pinaster
bark
1:2
500mL

ANISEED
Pimpinella anisum
fruit
1:1
200mL

ANISEED
Pimpinella anisum
fruit
1:1
500mL

Over a century of herbal medicine

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Reviews of articles on medicinal herbs

Tessa Finney-Brown

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

Turmeric's versatility

Yadav D, Yada S, Khar R, Mujeeb M, Akhtar M. 2013. Turmeric (*Curcuma longa* L.): A promising spice for phytochemical and pharmacological activities. *International Journal of Green Pharmacy* 7; 85-9.

Turmeric (*Curcuma longa*) has a long history of culinary use, giving many curries their yellow appearance; however, both practitioners and the general public are now aware of its value in herbal medicine. The University of Maryland states it has been used medicinally for over 4,000 years for a variety of conditions. This review of existing research provides an overview of the phytochemistry and pharmacological activities of turmeric, with several studies showing anti-inflammatory, antimicrobial, antifertility, anticancer, antidiabetic, antioxidant, hypolipidaemic, antivenom, antihepatotoxic, nephroprotective, anticoagulant and anti-HIV activity.

The anti-inflammatory effects of curcumin have been shown in several animal studies by the inhibition of induced paw oedema. A 50% reduction in oedema was achieved with a dose of 48 mg/kg body weight, with curcumin nearly as effective as cortisone and phenylbutazone at similar doses. In rats, a dose range of 20-80 mg/kg also decreased paw oedema and inflammation. Curcumin also inhibited formaldehyde induced arthritis in rats at a dose of 40 mg/kg, had a lower ulcerogenic index (0.60) than phenylbutazone (1.70) (an anti-inflammatory drug often used to treat arthritis and gout), and demonstrated no acute toxicity at doses up to 2 g/kg body weight. Curcumin also reduced mucosal injury in mice with experimentally-induced colitis with a dose of 50 mg/kg given for 10 days prior to induction of colitis.

Female rats given intraperitoneal injection of 4 mg total curcuminoids/kg/day for four days prior to rheumatoid arthritis induction saw a significant inhibition of joint inflammation in both the acute (75%) and chronic (68%) phases. A 30-fold higher dose to test oral absorption was given to rats four days prior to arthritis induction and saw reduced joint inflammation by 48% on the 3rd day of administration. Additionally, curcumin was shown to reduce inflammation in two rat models of experimentally-induced pancreatitis by markedly decreasing activation of nuclear factor-kappa B and activating protein-1. Curcumin also inhibited mRNA induction of interleukin-6, tumour necrosis factor-α and inducible nitric oxide synthetase in the pancreas.

Turmeric and curcumin (even at low dose) showed a cardioprotective and antioxidant action as well as reducing cholesterol and lipoprotein lowering cholesterol and triglyceride levels, decreasing susceptibility of low-density lipoprotein (LDL) to lipid peroxidation and inhibiting platelet aggregation in vivo.

A collection of studies have found that turmeric has a hepatoprotective action similar to silymarin, demonstrated through a variety of hepatotoxic insults.

Turmeric's hepatoprotective effect is attributed to its antioxidant properties and its ability to decrease the formation of pro-inflammatory cytokines. Additionally, turmeric extract and the essential oil of *C. longa* were shown to inhibit the growth of a variety of bacteria, parasites and pathogenic fungi in vivo.

This review demonstrates numerous actions which may explain the extensive use of turmeric in herbal medicine for a diverse range of conditions. The authors state that turmeric is highly regarded as a universal panacea in herbal medicine with a diverse pharmacological activity spectrum.

Kava for generalised anxiety disorder

Sarris J, Stough C, Teschke R, Wahid Z, Bousman C, Murray G, et al. 2013. Kava for the Treatment of Generalized Anxiety Disorder RCT: Analysis of Adverse Reactions, Liver Function, Addiction, and Sexual Effects. *Phytotherapy Research*, Published online in Wiley Online Library DOI: 10.1002/ptr.4916

Kava, the root of *Piper methysticum*, has been used in the islands of the South Pacific in traditional cultural ceremonies. The root is sliced and dried in the sun, pounded into a powder and then traditionally mixed and drunk from half a coconut. Its effects when consumed this way include an immediate numbing of the lips and tongue and a further relaxing sensation throughout the body during further consumption. The Fijians refer to kava's effects as being the opposite of alcohol and believe it is good for reproduction.

While traditional use, modern scientific evidence and clinical use show kava is an effective anxiolytic, this study used a pressed dried aqueous extract of kava tablet, standardised to contain 60mg kavalactones each, to assess whether kava displayed any withdrawal or addictive effects; if genetic polymorphisms of the cytochrome P450 2D6 (CYP 2D6) liver enzyme moderate any potential adverse effects; and if medicinal application of kava has any negative or beneficial effects on sexual

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function and experience.

This 6-week, double-blind, randomised controlled trial used 75 participants with diagnosed generalised anxiety disorder (GAD) and no co-morbid mood disorder. Participants were given kava tablets (120mg kavalactones per day) or placebo. The Hamilton Anxiety Rating Scale (HAMA) and Beck Anxiety Inventory (BAI) were used to assess severity of anxiety and baseline depression levels were also tested.

To the authors' knowledge, no studies have assessed the withdrawal or addiction issues with kava. This is a common clinical question and a valid concern. Kava has been shown in animals to increase dopamine in the nucleus accumbens. A blood test was taken prior to commencement to analyse the neurotransmitter gamma-aminobutyric acid (GABA), and noradrenalin transporter polymorphisms and CTP 2D6 single nucleotide polymorphisms as potential pharmacogenic markers moderating response and adverse effects, respectively. Only the kava group was re-analysed after study completion.

No significant difference was found upon assessment of potential addictive effects on the purpose designed addiction scale. Of those who took increased doses, 4% of the kava group took more tablets than instructed compared to 8% in the placebo group. Results showed no significant adverse effects and no significant negative effects across neurological, digestive, respiratory or cardiovascular functions. One case of allergy was seen in the placebo group, and one case of dermatitis and one case of minor stomach upset were seen in the kava group. 72% of the kava group noted improvement in areas such as stress, mood, sleep and somatisation. There was no difference between intermediate or extensive metabolisers with regard to any adverse effects.

Concerns over rare cases of hepatotoxicity have seen kava restricted over the years and withdrawn, although in Australia we currently have access to an aqueous extract (except in Western Australia, where the sale and supply is prohibited altogether). This study aimed to determine if genetic polymorphisms of the liver enzyme thought to be responsible for detoxifying kavalactones modify any potential side effects. As with other medications, those who are poor metabolisers may experience adverse effects differently to extensive metabolisers. Liver function tests including but not limited to albumin, total protein, bilirubin, alanine aminotransferase (ALT), aspartate aminotransferase (AST) and lactate dehydrogenase were performed to determine current hepatic function and possible hepatotoxicity or abnormal liver function.

Liver function tests conducted on weeks 1 and 7 revealed no significant differences and results were within standard range for both groups. No participant developed clinical signs of hepatic abnormality. One male participant in the kava group who was an extensive metaboliser according to CYP2D6 SNP analysis, had an isolated increase in y-glutamyl transpeptidase and a significantly higher ALT reading. Overall it was concluded that the relationship of CYP2D6 polymorphisms to abnormal liver function tests showed no differences between metabolisers.

Psychotropic pharmaceuticals such as antidepressants, mood stabilisers, antipsychotics and benzodiazapene have been documented to affect sexual function and experience. This study aimed to determine if this was the case for kava. Traditionally, kava was anecdotally reported as a sexual enhancer through traditional oral consumption, thus the authors considered it important to assess this as it had not been measured previously. Sexual function and experience was assessed with the Arizona Sexual Experience Scale (ASEX).

Results of ASEX showed kava caused no diminishment of sexual performance or enjoyment for either gender and actually improved sexual function among females in the kava group. There was a trend noted amongst males in kava group to increased difficulty in reaching orgasm. Overall, a decreased anxiety on the HAMA saw improvement of sexual function and enjoyment on the ASEX, and a significant increase in women's sex drive.

The authors showed for the first time that there was no deleterious effect on sexual function or pleasure during kava treatment but in fact a benefit for females, which they suggest may be due to the anxiolytic effect assisting in improved sexual satisfaction. The results from this trial support the use of standardised aqueous kava extracts as a reliable and non-addictive herbal medicine. With no adverse effects or withdrawals, nor negative liver impact, prescribing kava is a safe and effective treatment option for anxiety.

Garcinia cambogia for weight loss?

Heymsfield S, Allison D, Vasselli J, Pietrobelli A, Greenfield D, Nunez C. 1998. Garcinia cambogia (Hydroxycitric Acid) as a Potential Antiobesity Agent. *JAMA* 280; 1596-1600.

Garcinia cambogia has recently risen in popularity as a weight reduction treatment due to extensive advertisement on both the Internet and television. Recommended by Dr Oz and strongly consumer driven, *Garcinia cambogia* has fast become the newest weight loss fad. It claims to decrease appetite, mobilise fat, lower body weight and reduce fat mass.

Hydroxycitric acid (HCA) is the active constituent attributed to providing these results and it has become a popular ingredient in many commercial weight loss products with names such as Hydroxycut. HCA competitively inhibits the extra mitochondrial enzyme adenosine triphosphate-citrate (pro-3S)-lease, a citrate cleavage enzyme which plays an important role in de novo lipogenesis inhibition. HCA has been shown in vitro and in vivo to inhibit actions of the citrate cleavage enzyme and suppress de novo fatty acid synthesis as well as increase rates of hepatic glycogen synthesis, suppress food intake and decrease body weight.

Although experimental animal studies for weight

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loss showed promising results, the authors of this study chose to collectively review the 7 earlier human trials, which they considered to be limited and contradictory. Sample sizes were small, placebos were not included and measures of body lipid change were used inaccurately.

This 12-week randomised, double-blind placebo-controlled trial aimed to evaluate the efficacy of *Garcinia cambogia* for body weight and fat mass loss in overweight but otherwise healthy participants. Subjects were aged 18-65 years with a BMI of more than 27kg/m2 and at most 35kg/m2. Exclusion on the basis of previous dieting with weight loss in the past 6 months is of significance. Participants were given *Garcinia cambogia* active herbal compound of 50% hydroxycitric acid by chemical analysis, taken 3 times per day as two 500mg caplets 30 minutes prior to meals, giving a total 3000mg *Garcinia cambogia* and 1500mg of hydroxycitric acid, or placebo. Both groups were provided a high-fiber diet plan comprising 5040kJ/d with 20% fat, 50% carbohydrates and 30% protein, and were asked to maintain a stable exercise activity level.

Results showed that the participants in both groups lost a significant amount of weight during the 12 week period, but that there was no statistically significant difference between the groups. Body weight change differences remained non-significant; percentage of fat mass difference was also non-significant. Importantly, with *Garcinia cambogia* being so commercially popular, adverse events had no significant differences between the groups. In conclusion, *Garcinia cambogia* did not assist in weight loss or fat mass loss when compared with placebo and the authors stated that after all observations the role of *Garcinia cambogia* as a widely used herb for weight loss is not supported.

Boswellia reduces fatigue in MS patients

Majdinasab N, Siahpush A, Mohammadianinejad S, Fatemi S, Malayeri A, Alipour M. 2013. Clinical trial of *Boswellia serrate* on fatigue of patients with multiple sclerosis. *Ir J neurol* 12:1;10.

Multiple sclerosis (MS) is a perplexing and unpredictable disease with no single diagnostic test and a complex and variable symptom picture. MS Australia defines MS as a hardening of the tissue causing scars to form in the central nervous system as a result of the breakdown of myelin, resulting in impairment of motor, sensory and cognitive function. It is estimated 23 000 Australians have MS with three quarters being female. Symptoms are extensive but variable, and include bladder/bowel dysfunction, depression, headache, tremors and numbness. Fatigue is one of the most common symptoms, occurring in 90% of patients.

This placebo controlled study hypothesised that *Boswellia serrata* could be effective in lowering fatigue in patients with MS. Participants included 42 patients with diagnosed MS aged between 20 and 55, and with no occurrence of new attack or new severe emotional stress or depression. One group was given 900mg boswellia per day in capsule form, the other placebo. Fatigue was assessed before and after the study using the MS fatigue impact scale and analysed by paired t-test.

The results of this study showed the mean fatigue scale of the *Boswellia* group dropped from 55.14 to 48.43 whereas the placebo group actually increased from 51.43 to 53.00. The authors concluded that boswellia can lower the fatigue of multiple sclerosis patients significantly and attributed these findings to the anti-inflammatory effects of boswellia. This study reinforces the current clinical use of *Boswellia* as an important and effective anti-inflammatory.

Rhodiola and heat shock protein in marathon runners

Shanely R, Nieman D, Zwetsloot K, Knab A, Imagita H, Luo B, et al. 2013. Evaluation of Rhodiola rosea supplementation on skeletal muscle damage and inflammation in runners following a competitive marathon. *Brain, Behavior, and Immunity* http://dx.doi.org/10.1016/j.bbi.2013.09.005

Rhodiola rosea (RR) is a well-known and demonstrated adaptogenic herb which is widely used in clinical practice. Its constituents, rosavin, salidroside, syringin, triandrin, and tyrosol, are thought to confer its adaptogenic action. Adaptogens are defined in herbal medicine as natural substances which assist the body in adapting to stress by increasing nonspecific resistance to potentially harmful stimuli.

This study aimed to measure the influence of RR on exercise-induced muscle damage, delayed onset of muscle soreness (DOMS), plasma cytokines and extracellular heat shock protein 72 (eHSP72) in experienced runners completing a marathon. Marathons require prolonged intense exercise and endurance which causes a stress response in the body reflected by an increase in the plasma concentration of pro-inflammatory and anti-inflammatory cytokines. Damage is caused to the skeletal muscle fibre and damage to the sarcolemma allows leakage of proteins into the blood.

eHSP72 is increased in response to heat, hypoxia, inflammation, free-radical production, decreased glycogen and increased stress hormones. During this type of intense endurance exercise, eHSP72 is released into circulation from the liver and brain but not skeletal muscle, eliciting a pro-inflammatory immune response, while intracellular HSP72 (iHSP72) increases in skeletal muscle as an anti-inflammatory to minimise damage to the cells. Animal studies have shown that mice which over-express iHSP72 have less damage and recover quicker from injurious eccentric muscle contractions.

This randomised, double-blind, placebo-controlled trial saw experienced marathon runners aged 25-65 years receive RR at 600mg/day (one 300mg capsule twice daily) or placebo for 30 days prior to, the day of, and 7 days after the marathon. Blood samples were collected

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and vertical jump and DOMS assessed the day before, 15 minutes after, and 1.5 hours after marathon completion, and DOMS assessed for seven days post-marathon. The RR supplement was standardised to 5.2% of bioactive giving 11.3 mg of rosavins and 4.3mg of salidroside. Runners ingested food ad libitum during the race, which was later considered to be a limitation as not controlling carbohydrate intake could have resulted in variable cytokine responses between runners.

The purpose of this study was to measure the influence of RR on muscle function, markers of muscle damage including myoglobin and creatine phosphokinase, C-reactive protein, inflammatory cytokines and eHSP72 after running a marathon. The authors concluded that 600mg/day of RR did not alter eHSP72, muscle function, biomarkers of exercise induced skeletal muscle damage or inflammation, or DOMS. The adaptogenic benefit of RR in reducing muscle damage after strenuous exercise for athletes is reported and performance trials with RR have used a wide range of dosages and exercise regimes with variable results including cognitive function, mood, and performance enhancement.

Maca: superfood that may also protect gastric mucosa

Golbabapour S, Hajrezaie M, Hassandarvish P, Majid N, Hadi H, Nordin N et al. 2013. Acute toxicity and gastroprotective role of *M. pruriens* in ethanol-induced gastric mucosal injuries in rats. *BioMed Research International* Article ID 974185 http://dx.doi.org/10.1155/2013/974185

Maca (*Mucuna pruriens*) has become a popular superfood for numerous reasons, including its high protein and fibre content, full vitamin and mineral profile, and its reputation for increasing 'vitality', including enhancing energy and libido, especially in women, and reducing stress. The root of maca has been used as a food and traditional medicine for hundreds of years in Peru, where it naturally grows,. This study is of interest as it used the leaves as an extract rather than the powdered root which is the current widespread form utilised.

Maca is considered to be an effective treatment for free radical-mediated diseases such as diabetes, atherosclerosis and nervous disorders, as well as having procoagulant activity and benefits in the management of Parkinson's disease. It can also alleviate male infertility by suppressing psychological stress and improving semen quality through the regulation of steroidogenesis. Maca also displays hypocholesterolaemic, anti-inflammatory, diuretic, antioxidant and antimicrobial activity.

The present study investigated the gastroprotective effects of an ethanolic extract of maca leaves on ethanol-induced gastric mucosal injuries in rats. Peptic ulcers are predominately caused by *Helicobacter pylori* which increases the production of reactive oxygen species (ROS) and reactive nitrogen species (RNS) in the stomach resulting in oxidative stress on the gastric mucosa. Current ulcer treatments are ineffective against gastric mucosal lesions and often have side effects. Maca was used for its prior therapeutic actions and in particular its antimicrobial effects.

Forty-eight rats were divided into 8 groups of 6: negative control, extract control, ulcer control, reference control, and four experimental groups. They were fasted for 24 hours prior. As a pretreatment, the negative control and the ulcer control groups were orally administered carboxymethylcellulose (CMC). Omeprazole was given to the reference group as a gastroprotective drug, administered orally (20mg/kg). The extract of maca leaves was given orally to the extract control group (500mg/kg) and the experimental groups at a single dose of 62.5, 125, 250, and 500mg/kg. After 1 h, CMC was given orally to the negative and the extract control groups. The other groups received absolute ethanol. The rats were euthanised after 1h and the gastric mucosa was examined for damage.

The results showed that the rats pre-treated with omeprazole or *M. pruriens* had significantly smaller areas of gastric ulcers, inhibition of ulcer formation induced by ethanol and less gastric mucosal damage. The results were confirmed macroscopically. The study also showed that the plant is safe and has no toxicity when administered orally up to 5 g/kg. These results indicate that maca significantly suppressed the formation of ulcers and shows promising evidence in enhancing defensive mechanisms against hemorrhagic mucosal lesions. The authors concluded that *M. pruriens* showed a gastroprotective effect due to the preservation of gastric mucous secretion, increased production of Hsp70 protein, and increased antioxidant enzymes.

Black cohosh for menopause

Drewe J, Zimmermann C, Zahner C. 2013. The effect of *Cimicifuga racemosa* (CR) extracts Ze 450 in the treatment of climacteric complaints – an observational study. Phytomedicine 20:659-66.

This multi-centre observational study investigated the efficacy of *Cimicifuga racemosa* (CR) extract (Ze450) for menopausal complaints in 442 women (mean age 52.3) over 9 months. Gynaecologists and general practitioners were free to recommend dosages as they saw fit which resulted in the majority of the patients (372) being treated for 3 months with a high dose of 13mg/day of CR. Two smaller groups were dosed differently, 27 patients received a low dose of 6.5mg/day CR for 1 month and 23 patients received double the high dose for one month. The native extract dosages of 6.5mg and 13mg are equivalent to 40mg or 80mg of herb respectively.

A significant improvement in most symptoms such as hot flushes, insomnia, headache and nervousness was found in the high-dose majority ($p < 0.0001$). The other two smaller groups also found improvement (each $p<0.0001$).

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Reviews of medical journal articles

Tessa Finney Brown, Sarah Harvey

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.

Cystic fibrosis and the vitamin D paradox

Mailhot, G. 2012. Vitamin D bioavailability in cystic fibrosis: a cause for concern? *Nutr Rev* 70; 280 – 293.

Vitamin D is a nutrient which has garnered significant attention in medical and scientific realms over the last few years. There is an increasing understanding of the role of this hormone in a number of biological pathways, above and beyond traditional understandings of its endocrine and bone-regulating effects. Increasing evidence links it to the onset and progression of various chronic diseases, such as cancer, autoimmune disease and metabolic disorders.

Patients with cystic fibrosis (CF) suffer from an inherited mutation in a gene encoding the chloride channel cystic fibrosis transmembrane conductance regulator (CFTR). This dysfunction results in a wide variety of clinical symptoms affecting mainly the gastrointestinal tract and the lungs. Inadequate enzyme production leads to suboptimal nutritional status which occurs early and has significant impacts on the morbidity and mortality of the disease. Of the nutrient deficiencies that occur, vitamin D is by far the most common, with a prevalence of up to 90% in certain subgroups of CF patients.

A recent review on the topic in *Nutrition Reviews* has examined a number of studies and clarified the complex interactions between the disease and the vitamin. Cystic fibrosis patients have suboptimal fat absorption, which partly explains why vitamin D status is often low. However, they also seem to have suboptimal uptake of the nutrient when given high-dose supplementation, which suggests a primary defect in vitamin D bioavailability. In general, it seems that using supplements containing cholecalciferol, as compared to ergocalciferol, is more effective in correcting this deficiency.

Obtaining vitamin D through photoproduction is also problematic for many CF patients as many are on medications such as antibiotics and antifungals that induce photosensitivity. Thus, oral sources of the nutrient are often thought to be more suitable.

As well as problems with production and absorption, CF patients often struggle to maintain adequate stores of body weight which can lead to reduced adipose tissue being available to provide long-term storage depots for vitamin D. CFTR defects affect glycosylation of certain proteins in the blood, resulting in impaired vitamin D transport. Information also suggests that renal metabolism and urinary excretion of vitamin D may be affected in CF patients.

- The chronically low levels of active vitamin D in CF patients has scarcely been studied, but given the recent increase in knowledge of mechanisms of this compound, the author of the review suggests that it may affect the functioning of several body systems which then contributes to the morbidity and mortality of this disease. Among the effects, she specifically makes note of: links between higher vitamin D levels and more positive lung function in adult CF patients; vitamin D supplements being associated with lower rates of rejection after lung transplants;
- in patients with lower vitamin D levels, increased complications and hospitalisations post-surgery; vitamin D possibly playing a role in maintaining good immune function and helping to prevent lung infections in children and adults with CF; a possible role in CF-related diabetes; a possible link to increased intestinal inflammation in vitamin D insufficiency; vitamin D insufficiency contributing to the osteopenia and osteoporosis that invariable develop in CF patients.

The review concludes with a summary noting the many underlying factors that may contribute to vitamin D insufficiency in CF populations. It also suggests the potential aetiological role of vitamin D deficiency in a number of complications of CF, and recommends that management of serum levels play a key role in the management of this condition.

Myo-inositol benefits in PCOS

Genazzani A, Prati A, Santagni S, Ricchieri F, Chierchia E, Rattighieri E, Campedelli A, Simoncini T, Artini P. 2012. Differential insulin response to myo-inositol administration in obese polycystic ovary syndrome patients. *Gynecol Endocrinol* 28; 969-973.

Polycystic ovary syndrome (PCOS) is one of the most common endocrine disorders, estimated to affect up to 20% of women of reproductive age. It is a condition characterised by hyperandrogenism, chronic oligo-amenorrhoea, and polycystic ovarian morphology as demonstrated on imaging. Insulin resistance is a common feature of both overweight and normal weight women with PCOS, and is hypothesised to be involved in its aetiology. Insulin-sensitising drugs such as metformin are often used as part of the treatment of PCOS.

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Over the past decade, research has paid increasing attention to the role of inositol-phosphoglycan (IPG) mediators of insulin action, with growing evidence that a deficiency of D-chiro-inositol (DCI) containing IPG may be at the basis of insulin resistance. Due to this, researchers in Italy designed a trial to investigate whether supplements of myo-inositol would affect insulin sensitivity and hormonal parameters in PCOS patients.

Forty-two overweight women with PCOS were selected from the University of Modena's Gynecological Endocrinology Center to be enrolled in the study. All had normal prolactin levels and were excluded if they had any other endocrine disorder or had been on any hormone treatment in the last 6 months. The participants were divided into two groups based on fasting insulin levels. All participants received 2g myo-inositol and 200mcg of folic acid between 9am and 11am daily for 2 months.

At the conclusion of the study, there was a significant reduction in luteinizing hormone to follicle stimulating hormone (LH/FSH) ratio, FSH, prolactin, androstenidione, testosterone, insulin and body mass index (BMI) compared to baseline. There was also a significant increase in the glucose to insulin ratio. While both groups had reductions of baseline fasting insulin levels, these were only statistically significant in the group which had the highest insulin levels initially. No side effects or adverse effects were seen in any of the patients in the study.

These results suggest a strongly beneficial effect for myo-inositol in the treatment of PCOS and, potentially, other insulin resistant conditions.

The wonders of walnuts

Guasch-Ferré M, Bulló M, Martínez-González M, et al. 2013. Frequency of nut consumption and mortality risk in the PREDIMED nutrition intervention trial. BMC Med 11; 164.

Multiple prospective and epidemiological studies have assessed the link between Mediterranean-type diets and coronary heart disease mortality. One factor that has been identified as particularly protective in these dietary patterns is the consumption of nuts, which have also been linked to a small protective effect on all-cause and cancer mortality.

In an attempt to discover if nuts really are an elixir of life, researchers in Spain undertook a prospective study examining nut consumption and mortality in Spanish individuals at high risk of cardiovascular disease. 7216 men and women between the ages of 55 and 80 were evaluated, and randomised to one of three interventions: a Mediterranean diet; a Mediterranean diet supplemented with nuts or olive oil; and a standard control diet. Nut (specifically walnut) consumption at baseline was measured, and then mortality was ascertained by linkage to the National Death Index and examination of medical records. Whilst none of the participants in the study had cardiovascular disease (CVD) at the time of enrolment, they were assessed as high risk due to the presence of type 2 diabetes mellitus or the presence of 3 key risk factors for CVD, such as smoking, a positive family history and others.

The average follow-up period was 4.8 years – during this time there were a total of 323 deaths, 81 from cardiovascular causes and 130 from cancer-related illness. Overall, the subjects consuming more than 3 servings of nuts per week had a 39% lower all-cause mortality risk. Note that for the purposes of the study, one serving of nuts was considered to be 28g. This group also exhibited lower rates of cancer and cardiovascular mortality. Upon subgroup analysis it was shown that consumption of any nuts was linked to lower all-cause and cardiovascular mortality, but only walnuts were shown to reduce rates of cancer deaths.

These protective effects may be due to the high mineral content of nuts, as well as phytochemicals such as phenolic acids, phytosterols and polyphenols. Walnuts in particular have a high content of alpha-linolenic acid and may have higher bioavailability of the phytochemicals mentioned previously (as they are consumed in their skins).

The results of this study confirm earlier reports of benefit, and suggest that when practitioners are counselling patients about nut consumption to help prevent CVD and cancer mortality, they may wish to educate about the greater benefits of walnuts.

Early supplementation of probiotics and effects on eczema and atopy

Wickens K, Stanley T, Mitchell E, Barthow C, Fitzharris P, Purdie G, Siebers R, Black P Crane J. 2013. Early supplementation with *Lactobacillus rhamnosus* HN001 reduces eczema prevalence to 6 years: does it also reduce atopic sensitization? *Clinical & Experimental Allergy* 43; 1048–1057.

Whilst many studies have been conducted on probiotics for various conditions, and many have demonstrated health benefits, the role of probiotic treatment in prevention of atopy is still far from clear. Understandably, results may vary depending on the dose, timing, duration and specific strain of probiotic used. This leaves practitioners with many questions about the optimal dosing of such supplements during pregnancy and early life.

A recent study in Australian and New Zealand mothers and infants may shed some more light on these particular questions. Researchers conducted a double-blind, randomised, placebo controlled trial in a high-risk birth cohort. Mothers were given *Lactobacillus rhamnosus* HN001 (HN001) at a dose of 6 x 10^9 cfu/day or *Bifidobacterium animalis* subsp *lactis* HN019 (HN019) at a dose of 9 x 10^9 cfu/day. They took this from 35 weeks of gestation, and continued through to 6 months of breastfeeding. The child was also supplemented with probiotics at the above doses from birth until 2 years of age.

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The primary outcome measure was eczema prevalence at 2, 4 and 6 years of age; other outcomes assessed were eczema severity, skin prick test (SPT) reactions to common allergens, serum cytokine levels, and prevalence of wheeze and rhinoconjunctivitis.

Results showed that HN019 had no significant effects on any outcome measure. However, HN001 use was associated with significantly lower rates of eczema and SPT sensitisation when compared to placebo. This provides evidence for the efficacy of *L. rhamnosus* HN001 in preventing the development of atopy and eczema in high-risk infants up to the age of 6 years.

Practitioners may wish to implement this treatment in pregnant mothers at 35 weeks, and continue to dose her until the infant is 6 months (if breast feeding). Infants should also be started on the probiotic from birth and continued until the age of 2. The study highlights the importance of choosing the right strains of probiotic when treating patients for specific goals. *B. animalis* subsp *lactis* HN019 is unlikely to be useful in preventing these types of conditions when given at this dose in this type of regime.

Review of vitamin E bioavailability

Borel P, Preveraud D, Desmarchelier C. 2013. Bioavailability of vitamin E in humans: an update. *Nutr Rev* 71; 319 – 331.

Vitamin E is a key lipid soluble antioxidant which exerts multiple roles in the body, including modulation of gene expression, inhibition of cell proliferation, monocyte adhesion and platelet aggregation, as well as regulation of bone mass. The term refers to eight compounds, four tocopherols (α, β, ϒ and δ) and four tocotrienols (α, β, ϒ and δ), which possess the biological activity of α-tocopherol. The main isomers in the Western diet are α- and ϒ- tocopherol.

Given that vitamin E is used heavily as an antioxidant in the food industry and occurs in multiple supplements (over 10% of the US adult population take a supplement containing vitamin E), recent interest has focused on which of the eight isomers is the best form to use. Despite the potential benefit of vitamin E in various illnesses having been studied extensively, little is known about mechanisms of absorption, nor factors that affect its efficacy and bioavailability.

For this reason, a recent meta-analysis was carried out, examining the factors that various studies have shown to affect vitamin E concentrations in the blood after administration of a standard dose of the supplement. This was understood to be a surrogate marker for bioavailability of the compound. Overall, factors shown to affect Vitamin E absorption included:

- Species of vitamin E: while the small number of studies evaluated failed to show a clear conclusion, some suggested preferential absorption of α-tocopherol.
- Molecular linkage: absorption of both free and esterified forms is similar (in patients with normal gastrointestinal enzyme function).
- Amount of vitamin E consumed in a meal: there is no evidence that efficiency of vitamin E absorption decreases with increasing doses.
- Matrix in which vitamin E is incorporated: this is a key factor in the absorption of vitamin E from foods, but there is little data to suggest how vitamin E in vegetable oils (a major source in the diet) is affected by the food matrix. Vitamin E bioavailability has been shown to be higher for ground vs. whole nuts and almost 100% from bananas, bread and lettuce.
- Effectors of absorption and bioconversion:
    - Dietary lipids enhance bioavailability, with medium chain triglycerides possibly being more beneficial than long chain triglycerides due to oxidation of polyunsaturated fatty acids (PUFAs).
    - Conjugated linolenic acid leads to increases in Vitamin E in liver and kidney, not related to increased bioavailability.
    - Some evidence suggests that phosphatidylcholine inhibits absorption, but clinical studies in humans are needed.
    - Dietary fibre at normal levels does not seem to affect bioavailability.
    - Animal studies suggest that cholesterol absorption inhibitors may also lower Vitamin E absorption, but human clinical studies are required.
- Nutrient status of the host: hypothesised to affect uptake, but no studies have been done to assess this.
- Genetic factors: various polymorphisms in genes affecting vitamin E or lipid absorption may affect bioavailability, but further research is needed to assess how to use this data clinically.
- Host related factors:
    - Age: absorption is similar across the lifespan, except that large doses of α-tocopherol may be less efficiently absorbed in the elderly.
    - Health disorders that impair fat absorption lead to impaired vitamin E bioavailability (e.g. coeliac disease, obstructive jaundice, cystic fibrosis).
    - Chemoradiation treatment may impair absorption.

In both Europe and America, many adults fail to meet the recommended daily intake (RDI) for this vitamin, which suggests that Australian adults may be similar. In addition, dietary recommendations to increase consumption of mono- and poly-unsaturated fatty acids may increase the intake of Vitamin E. If practitioners are considering vitamin E supplementation, in order to get the greatest efficacy, they should consider the factors above which may affect bioavailability.

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Combination therapy increases BDM in osteoporotic models

Abdul-Majeed S, Mohamed N, Soelaiman I. 2012. Effects of Tocotrienol and Lovastatin Combination on Osteoblast and Osteoclast Activity in Estrogen-Deficient Osteoporosis *Evidence Based Comp & Alt Med* doi:10.1155/2012/960742

Osteoporosis is a very common, silent and age-related disorder that is a major public health problem. Patients suffer decreases in bone density and disruption in the normal micro-architecture of bone, eventually resulting in fragility, fractures and falls. The pathogenesis of the condition involves decreased osteoblastic activity relative to osteoclastic activity, influenced by a multitude of factors such as vitamin D levels, parathyroid hormone, oestrogens and bone loading. Current therapies are targeted at reducing osteoclastic activity, thus addressing bone loss, but are not suitable for increasing bone volume.

Previous studies have demonstrated that HMGCoA reductase inhibitors (statins), when given in high doses, may stimulate bone formation in rodents. Observational studies in humans, however, have had mixed results. Other murine studies have shown that tocotrienols have both anabolic and catabolic effects on bone.

To establish the activity of these two agents in combination, researchers in Malaysia designed a murine study. They took 48 female Sprague-Dawley rats and divided them into 6 groups:

1. Baseline control
2. Sham-operated control
3. Ovariectomised control
4. Ovariectomised + 11mg/kg lovastatin
5. Ovariectomised + 60mg/kg delta-tocotrienol
6. Ovariectomised + 60mg/kg delta-tocotrienol + 11mg/kg lovastatin

Treatments were given daily for 8 weeks, and then a number of biochemical and static bone histomorphometric parameters were assessed.

Delta-tocotrienol and lovastatin in combination significantly increased bone formation in the ovariectomised rats (simulation of a post-menopausal population) and reduced bone resorption compared to the other groups. Researchers suggested that the interventions thus had synergistic (additive) effects and showed promise as an anti-osteoporotic agent in patient groups at risk of both hypercholesterolaemia and osteoporosis (e.g. postmenopausal women).

Zinc as an adjunct for pneumonia treatment

Wadhwa N, Chandran A, Aneja S, Lodha R, Kabra S, Chaturvedi M, Sodhi J, Fitzwater S, Chandra J, Rath B, Kainth U, Saini S, Black R, Santosham M, Bhatnagar S. 2013. Efficacy of zinc given as an adjunct in the treatment of severe and very severe pneumonia in hospitalized children 2–24 mo of age: a randomized, double-blind, placebo-controlled trial. *Am J Clin Nutr* 97; 1387–94.

Around the world, pneumonia is a leading cause of death in immunocompromised populations, such as the elderly and young children. In India, the country with the single highest global burden of the condition, it is estimated that 370 000 children die of pneumonia each year. Strategies to reduce pneumonia mortality centre around community-based standardised care, and it is estimated that these may reduce the mortality rate by up to 70%.

In addition, many children in India and other low- and middle-income countries are known to suffer from zinc deficiency. This nutrient plays key roles in the immune response to infections and is essential for both the adaptive and innate immune systems. It is recommended by WHO as an adjunctive therapy for treating diarrhoea, but results of clinical studies on the role of zinc in respiratory infection have been mixed.

This study evaluated the role of zinc as an adjunct to antibiotics in the treatment of children hospitalized for severe or very severe pneumonia. The researchers conducted a double-blind, randomised, placebo-controlled trial on 550 children aged 2-24 months. They enrolled only children who had severe or very severe pneumonia, and then randomised groups within each hospital and within the two pneumonia strata. Patients received either one tablet of zinc (10mg elemental) or a placebo, dissolved in distilled water. The dosing was 12-hourly until recovery, or the completion of 14 days, whichever was sooner.

After completion of the trial, results indicated that the time to recovery was similar in both groups. In stratified subgroup analysis, there was a reduced time to recovery in the children with severe pneumonia, but this was no longer statistically significant after adjusting for the severely underweight children in both groups. Overall, the intervention showed no significant benefit in using this dose of zinc as an adjunct in treatment of severe to very severe pneumonia. The researchers suggest further study be done in specific subgroups of children with very severe illness.

Seaweed booster for the flu vaccine

Negishi H, Mori M, Mori H, Yamori Y. 2013. Supplementation of Elderly Japanese Men and Women with Fucoidan from Seaweed Increases Immune Responses to Seasonal Influenza Vaccination. J Nutr. doi: 10.3945/jn.113.179036.

The elderly are commonly an immunocompromised group known to be at risk of diseases such as influenza. In many countries, including Australia, vaccinations are recommended for this group for protection against the 'flu. However, the elderly are also known to have an inadequate response to the vaccine.

Seaweed, a common food substance in Japan, has previously been speculated to have positive effects on health, due to its ubiquity in the Japanese diet and the renowned longevity of this group of people. Recent

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studies have demonstrated water extract of seaweed to assist in improving herpes simplex symptoms, and fucoidans (polysaccharides in seaweed) reportedly have physiological effects on immunity including antiviral, anti-inflammatory and antitumour effects. Mekabu fucoidan (MF) is a specific sulphated polysaccharide extracted from the edible seaweed *Undaria pinnatifida.* It has been proven to enhance natural killer cell activity, increase neutralising antibody production in mucosa and blood, and inhibit viral growth.

A recent study examined whether MF would have an effect on immune responses to influenza vaccination in elderly Japanese men and women. 70 study participants were randomised into 2 groups, one of which received placebo and the other MF (300mg/d) for four weeks. They were then given a trivalent seasonal influenza vaccine.

After 5 and 20 weeks, the study participants had blood samples taken to assess hemagglutination inhibition titre and natural killer (NK) cell activity. Those who were taking the active seaweed supplement had higher antibody titres against all three strains of the 'flu in the vaccine than volunteers in the placebo group. In the active group, there was also a rise in NK cell activity nine weeks after MF intake, while no such rise was noted in the placebo group.

This study suggests that MF supplementation (or possibly high levels of seaweed consumption) in the elderly for one month prior to an influenza vaccine may enhance their immune responsiveness to the immunisation, thus improving its efficacy and protection against contracting seasonal strains of influenza.

Herbal treatment for hepatotoxicity associated with high fat diet, methamphetamine use and anxiety: a case study *References continued from page 204*

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MedPlant - Black cohosh for menopause *continued from page 209*

In the second phase of the study, treatment was either continued at high dose or reduced to low dose for a further 6 months. Choice of treatment and dosage was still at the discretion of the medical practitioner. Continuation of treatment with both doses was found to reduce total menopausal symptoms (each $p<0.0001$); however, significant reductions in the low-dose group were only recorded for psychological and somatic symptoms such as nervousness, insomnia, fatigue and melancholia.

It was noted that the small group of 23 patients in Phases 1 and 2 treated with double the high dose did not show any greater reduction in symptoms than those in the high-dose group, indicating that the increase in Ze450 dose beyond 13mg daily may not increase effectiveness. The dosage of CR usually used in Australia is equivalent to 42.25mg, which equates to the low dose used in this trial. The study was undertaken by employees of Max Zeller Soehne AG who also funded it and provided the CR.

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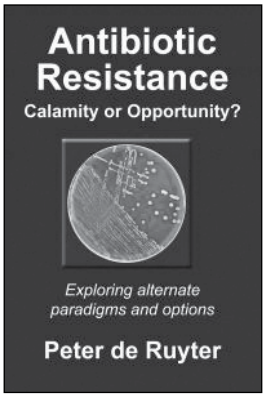
Book review



Antibiotic resistance – calamity or opportunity? Exploring alternate paradigms and options

by Peter De Ruyter

Reviewed by Kathy Harris

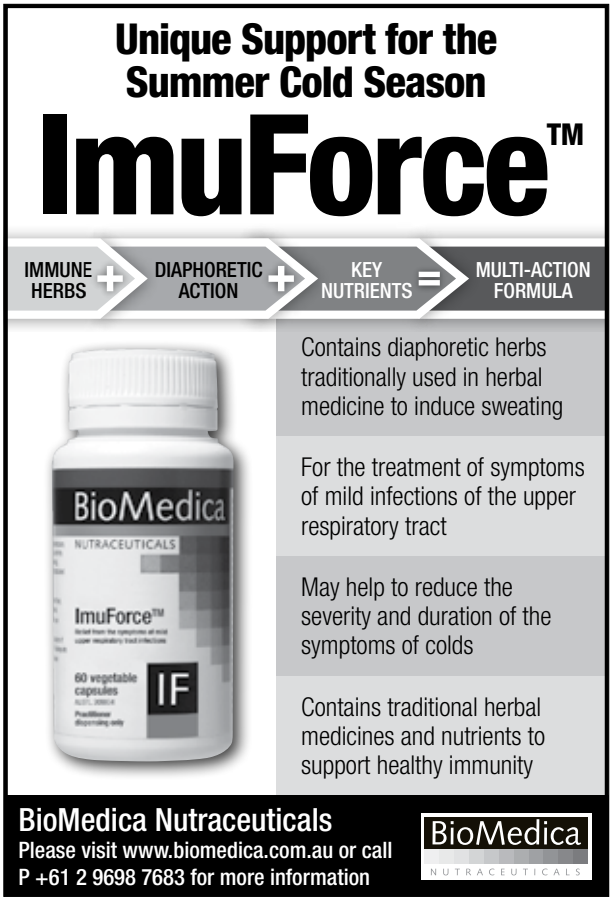
This self-published book, also available as an eBook, is well pitched to those who want to take responsibility for their wellbeing and not rely solely on orthodox medicine. Although the title implies that the book is only about antibiotic resistance, it is about so much more. The focus is on self-empowerment and prevention, and working with the life force to handle infections from a holistic perspective and regain and maintain a better level of health.

Students and new practitioners, who may be contemplating the philosophy that underpins their recommendations to their families and patients and the overarching paradigm that frames their beliefs, will find this book rich food for thought. Naturopathic clients could certainly benefit from reading it, which would also reduce the need for practitioners to explain the rationale for their recommendations. There is a great deal of sound advice that is based on traditional herbal wisdom. The book serves to remind us of the value of combining the scientific evidence base with traditional wisdom.

Peter de Ruyter has been in clinical practice for over three decades, during which time 25% of his practice has involved dealing with HIV/AIDS clients. Prior to that he was a Registered Nurse with a Bachelor of Science and worked in pathology. Thus, he has an extensiveexperience working with patients with serious infections through focusing on their life force and quality of life from a multifaceted perspective. It is apparent that this is a book that Peter had to write. His depth and breadth of clinical experience and his repeated frustrations with the limitations of orthodox medicine's reductionist viewpoint led to a journey that is the substance of this book.

The 204-page book is laid out in a rather conversational and meandering style, with a logical flow and effective use of metaphors. The title is a little wordy and could have conveyed more about the gems that lie within the pages; however, antibiotic resistance is a very topical and concerning issue. The chapter titles do not always align with the content, but the information therein is good food for thought. The author covers some controversial subjects, such as in Chapter 15: "Dilute Hydrochloric Acid – controversial but effective". Chapter 17, the final chapter, contains a summary of the issues explored in the book, along with the author's conclusions. There are 44 references and two appendices which highlight Peter's other eBooks and websites.

There are pages where I would have liked to have seen disclaimers included under herbal recommendations e.g. "*Best undertaken in conjunction with a naturopath or Western medical herbalist*", but none are evident. It is concerning that in today's world, people tend to order natural remedies online, many of which have cautions, contraindications or herb-drug interactions. Hopefully, many readers will come across this book because they are already under the care of a health professional. Our patients may need a prod to motivate them to read it, but once they get to Chapter 4, they will undoubtedly feel empowered and engaged.



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AJHM based CPE Questionaire

The AJHM 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 Herbal Medicine*. 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 – AJHM 25(4)

1. Turmeric has been found to:

a) Reduce mucosal damage in mice with induced colitis.
b) Inhibit a variety of bacteria, parasites and pathogenic fungi.
c) Have cardioprotective and antioxidant activities including lowering cholesterol.
d) All of the above.

2. Which of the following is correct?

a) Kava diminished sexual performance and enjoyment in both genders.
b) Kava increased anxiety in participants.
c) No participant in the study developed clinical signs of hepatic abnormality.
d) Kava was found to exhibit withdrawal effects in participants.

3. Which is the following is incorrect regarding *Garcinia cambogia*?

a) This study has shown *G. cambogia* to be an effective and reliable weight loss supplement.
b) The active ingredient in *G. cambogia* is hydroxycitric acid.
c) *G. cambogia* has been shown in vitro and in vivo to inhibit the action of the citrate cleavage enzyme.
d) None of the above.

4. Which is the following is correct regarding *Mucuna pruriens*?

a) Maca was used in this study as an aqueous extract as opposed to an ethanol extract.
b) Maca significantly suppressed the formation or ulcers and shows promising evidence in enhancing defensive mechanisms against haemorrhagic mucosal lesions.
c) The active constituents in maca are kavalactones.
d) This study confirms maca as an effective treatment for libido enhancement in women.

Medical science questions – AJHM 25(4)

1. From the information given above, which of the following is the most correct?

a) Myo-inositol and folate when combined had a greater effect on PCOS symptoms than folate alone.
b) Folate may help to reduce insulin resistance in PCOS.
c) Myo-inositol may help to reduce insulin resistance in PCOS.
d) Myo-inositol and folate may help to reduce insulin resistance in PCOS.

2. From the information given above, which of the following is the most correct?

a) Walnuts were shown to be beneficial in helping to prevent all-cause mortality, as well as mortality from CVD and cancer.
b) Walnuts increased the risk of cancer mortality, but decreased the risk of cardiovascular mortality.
c) Although nuts were shown to be beneficial for mortality, olive oil was shown to have a greater effect.
d) A low fat diet should be recommended for those wishing to avoid CVD.

3. From the information given above, which of the following is the most correct?

a) Any probiotics will be effective at preventing atopy in children, as long as they are given at the right time.
b) Only *B. animalis subsp lactis* was shown to have benefit in preventing eczema development.
c) Optimal dosing of to prevent eczema and atopy in high-risk infants should begin in pregnancy and be continued in mother and child post-partum.
d) *L. rhamnosus* HN001 seems to help prevent asthma in high-risk infants.

4. From the information given above, which of the following is the most correct?

a) Vitamin E is easily absorbed from all foods.
b) Although it is not conclusive, α-tocopherol may be the most bioavailable form of vitamin E.
c) Age plays a significant role in how much vitamin E a person can absorb.
d) Walnuts are the most bioavailable source of vitamin E.

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- A brief profile of the author should be included.

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