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MEDICINAL CANNABIS:

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What topics would you like to see covered in FX Medicine®?
Email your suggestions to editor@fit.net.au and we will endeavour to include in future editions.

FX Medicine® is published quarterly by BioCeuticals. It contains articles written by healthcare professionals and professional editorial staff for complementary medicine practitioners. Editorial content is selected by the Editor, with advice from the Editorial Board, with the view of providing the reader with practical and relevant information in regards to the use of complementary medicines.

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This issue of *FX Medicine* is packed full of helpful information, including our Stress and Mood feature section (page 10). Read up on the underlying causes and treatment strategies for pyrrole disorder; how neuroinflammation contributes to brain and mood health; and how our gut microbiota may be connected to depression and anxiety.

The *FX Medicine* team would love to hear from you! Email us at editor@fit.net.au with your feedback and article suggestions.

Happy reading,

Jennifer Joseph
Editor

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Research Insights

Melissa Peterson,
AdvDipHSc(Nat) GradCertEvBdPrac

EPA/DHA: recommended therapy for NAFLD

The beneficial effect of omega-3 polyunsaturated fatty acids, EPA and DHA, on non-alcoholic fatty liver disease (NAFLD) is substantial, according to data collated in a recent meta-analysis.

After a systematic literature search, 10 eligible case-control studies and 11 randomised controlled trials (RCTs) were reviewed for the effect of these fatty acids on alanine aminotransferase (ALT), aspartate aminotransferase (AST), liver fat and triglyceride levels, in NAFLD.

In the case-control studies, DHA levels were significantly higher in the liver and blood of the control subjects compared to those with NAFLD.

In the RCTs, essential fatty acid (EFA) therapy, especially DHA, significantly reduced ALT, AST and triglyceride concentrations, while marginally reducing liver fat content.

This review provides considerable evidence of these EFAs for the treatment of NAFLD.

Guo XF, Yang B, Tang J, et al. Fatty acid and non-alcoholic fatty liver disease: meta-analyses of case-control and randomized controlled trials. Clin Nutr 2017; doi: 10.1016/j.clnu.2017.01.003

Meta-analysis confirms hypericum use for depression

Conflicting data on the benefits and risks of *Hypericum perforatum* (St John's wort) and the lack of a recent meta-analysis, prompted reviewers to conduct a meta-analysis of the clinical data behind this popular herb used in depression.

Multiple database searches found 27 relevant trials, totalling 3808 patients, which compared the clinical response of St John's wort with serotonin selective reuptake inhibitors (SSRIs).

Response and remission rate, along with safety, were comparable to the SSRIs, with the benefit of a significantly lower dropout rate in the herbal groups.

The results showed this herb has significant clinical efficacy in reducing mild to moderate depressive symptoms. Longer-term studies and those focused on severe depression would provide further evidence.

Ng QX, Venkatanarayanan N, Ho CY. Clinical use of *Hypericum perforatum* (St John's wort) in depression: a meta-analysis. J Affect Disord 2017;210:211-221.

Zinc – a simple treatment for PMS

In a recent randomised controlled trial, zinc supplementation significantly improved moderate to severe premenstrual syndrome (PMS) symptoms.

This prospective trial used a screening tool and questionnaire to analyse the symptoms of 142 women, aged 20-35 years, with PMS.

The treatment group took 50mg elemental zinc (in sulfate form) from day 16 of their menstrual cycle to the second day of their next cycle, for three months.

The prevalence of PMS significantly decreased to 9.5% in the first month, 6% in the second month and 2.6% in the third month. The control group rates remained around 13-14% for the trial period.

Additionally, health-related quality of life scores were significantly improved with the zinc supplementation.

Siahbazi S, Behboudi-Gandevani S, Moghaddam-Banaem L, et al. Effect of zinc sulfate supplementation on premenstrual syndrome and health-related quality of life: clinical randomized controlled trial. J Obstet Gynaecol Res 2017; doi: 10.1111/jog.13299

Supplements benefit stressed women

In a systematic review, several nutritional compounds demonstrated efficacy in reducing psychological and physiological stress and anxiety in women.

Due to high levels of stress on women in society and the widespread use of dietary supplements, researchers designed a review of the current literature to identify the impact of EFAs, B vitamins, vitamin C and magnesium on stress and anxiety levels.

The 14 studies included in the review demonstrated that EFAs may be effective in reducing:

- perceived stress
- salivary cortisol levels in pregnancy
- anxiety in PMS and menopause (when depression is absent).

Vitamin B6 was found to reduce anxiety in older women, and when combined with magnesium, reduced premenstrual anxiety. High-dose sustained release vitamin C reduced anxiety and blood pressure in women subjected to stress.

This review provides support for the clinical use of these supplements in managing female stress and anxiety.

McCabe D, Lisy K, Lockwood C, et al. The impact of essential fatty acid, B vitamins, vitamin C, magnesium and zinc supplementation on stress levels in women: a systematic review. JBI Database System Rev Implement Rep 2017;15(2):402-453.

Magnesium needed for obese women

Low magnesium intake is linked to increased oxidative stress in obese women, even though the plasma and erythrocyte magnesium levels may be in the normal range, according to a recent study.

In a cross-sectional study, 83 women aged 20-50 years were divided into an obese group and a non-obese control group. Magnesium intake was calculated from a three-day diary record with fasting plasma and erythrocyte concentrations measured. Theobarbituric acid reactive substances (TBARS), biomarkers for oxidative stress, were also determined.

In both groups, the magnesium dietary intake was lower than the recommended daily allowance (RDA) and the estimated average requirement (EAR), with plasma and erythrocyte magnesium levels in the normal range.

However, an analysis between the biochemical parameters of magnesium and the plasma TBARS found a significant negative correlation between erythrocyte levels and lipid peroxidation in the obese women. Therefore, although the body controlled the erythrocyte concentration maintaining a homeostatic normal range, hypomagnesium may still be evident and a cause of increased oxidative stress in this group.

Morais JB, Severo JS, de Oliveira AR, et al. Magnesium status and its association with oxidative stress in obese women. Biol Trace Elem Res 2017;175(2):306-311.

Higher dose B vitamins for schizophrenia

A review of randomised trials show B vitamins may significantly reduce the symptoms of schizophrenia.

To confirm if nutritional supplements may be effective in restoring nutritional deficits, reducing oxidative stress, or modulating neurological pathways in schizophrenia, researchers undertook a large-scale review of the existing research.

They analysed 18 eligible randomised controlled trials, totalling 832 psychiatric patients, and found that B vitamin supplementation (including B6 and B12), either singularly or in combination, reduced psychiatric symptoms significantly more than the control groups. The benefits were the greatest when the vitamins were taken early in the disease progression and in high doses.

Firth J, Stubbs B, Sarris J, et al. The effects of vitamin and mineral supplementation on symptoms of schizophrenia: a systematic review and meta-analysis. Psychological Medicine 2017:1-13.
Sandoiu A. B vitamins may improve schizophrenia symptoms. Medical News Today 2017. Viewed 27 Feb 2017, http://www.medicalnewstoday.com/articles/315866.php

Immune boosters

Eating well, exercising regularly, resting and keeping germs at bay are four of the most effective ways to avoid colds and winter ills. But for those patients who need extra support to bolster their immune system, the BioCeuticals Immunity Range has something for everyone.

ArmaForce 60 tabs RRP $33.95, 120 tabs RRP $61.50

The ultimate supplement for the cooler months, ArmaForce is a comprehensive formula combining the herbal and nutritional ingredients andrographis, echinacea, olive leaf, vitamin C and zinc. It has been scientifically formulated to provide relief of symptoms and decrease the duration of upper respiratory tract infections and colds. ArmaForce supplies nutritional support for healthy immune function. Each tablet provides 62.5mg andrographolides from a standardised extract of andrographis to help support healthy immune function and provide relief from the symptoms of the common cold.

SUPPORTS HEALTHY IMMUNE FUNCTION

Ultra Potent-C® 200g oral powder RRP $36.95, 500g oral powder RRP $67.50

Ultra Potent-C combines a high dose of various forms of vitamin C, together with zinc, vitamin E, betacarotene and rutin in an easy-to-mix-and-drink oral powder for immune system and antioxidant support. With 2.45g of total vitamin C per 4g dose, the formula contains a blend of three ascorbates providing optimal delivery of vitamin C with minimal gastrointestinal discomfort. It contains zinc chelated to an amino acid; known to enhance zinc absorption. Vitamin C is involved in minor wound-healing, the cross-linking of collagen, and the synthesis of hormones and neurotransmitters. With a natural orange flavour, it is vegan and vegetarian friendly.

BLEND OF ASCORBATES FOR DIGESTIVE EASE

ViroGuard 60 caps RRP $37.50, 30 caps RRP $17.95

ViroGuard is a unique combination of micronutrients and herbs that provide support for healthy immune function. ViroGuard has been formulated to help relieve the frequency, duration and severity of cold sores. It also relieves the symptoms of cold sores, and supports and maintains healthy immune function. The formula includes *Melissa officinalis*, naturally high in rosmarinic acid, the highly bioavailable zinc amino acid chelate, as well as *Echinacea purpurea*, traditionally used in North American herbal medicine to support a healthy immune system.

NEW 30 CAPSULE BLISTER PACK!

Zinc Sustain 60 tabs RRP $19.50, 120 tabs RRP $33.95

Zinc Sustain features 30mg of zinc in an amino acid chelate form and cofactors to assist with its absorption. Zinc has many physiological roles and is involved in the major metabolic pathways of the body. The formula includes magnesium as well as vitamins A, B6 and C which are important cofactors for zinc absorption. Zinc and vitamins A and C have demonstrated roles in the maintenance of a healthy immune system and healthy skin. May assist in the management of minor wounds, cuts, scratches and abrasions. People with increased needs for zinc may include adolescents, pregnant and lactating women, and the elderly.

CONTAINS HIGH DOSE ZINC

The legalisation of medicinal cannabis in Australia: where are we now?

Justin Sinclair, MHerbMed BHSC ND

If you're one of the millions of people who thought cannabis was now easily available in Australia for medical purposes, think again – for not everything is as it appears in the evening news...

Just a few years back things looked promising; the impetus to legalise the plant as a medicine had begun in earnest. Huge media attention was focused on ex-nurse Lucy Haslam and her son Dan, whose story captured the public's imagination. Dan, in his early 20s, was a young man struggling with nausea and vomiting induced by the chemotherapy used to fight his inoperable bowel cancer. This was in 2013, and seeing the dramatic relief cannabis gave him, Lucy and Dan together with dad Lou, a retired NSW Police Officer in drug enforcement, started campaigning for the herb's re-introduction to the physician's armamentarium.

Tragically, Dan died in 2015, but Lucy had already founded United in Compassion (UIC), a not-for-profit advocacy group whose primary mission was – and still is – to win patient access to medicinal cannabis (MC) in a manner that is safe, affordable, equitable, expeditious and favourable for all who need it. The lobbying of politicians at state, territory and federal levels soon followed and in November 2014, Lucy hosted the inaugural UIC Medicinal Cannabis Symposium in Tamworth, NSW. Experts in the field from around the world flew in to discuss the plant's many therapeutic properties, and how it was being used widely and with huge success overseas. Largely funded by Mike Baird, then NSW Premier, the event also attracted a clutch of other politicians including Green Party leader Senator Richard Di Natale, himself a qualified medical practitioner.

That same year, Senator Di Natale, with support from Senators Macdonald, Leyonhjelm and Urquhart, proposed new legislation to the senate – the Regulator of Medicinal Cannabis Bill 2014.[1] It outlined a system for regulating MC outside the jurisdiction of the Government's normal regulator, the Therapeutic Goods Administration (TGA), seeking instead to create a stand-alone, single-purpose body responsible for research, licensing, manufacture, cultivation, supply, and import/export of MC with the idea Australia would eventually have a local supply. This 'national' regulator was to be a 'one stop shop' for everything MC, including the critical matter of patient access.

In February 2015, the bill was referred to the senate's Legal and Constitutional Affairs Legislation Committee for review and counsel. After over six months of vigorous debate and consultation across a variety of areas and disciplines, the committee recommended the bill be passed into law. However, the Australian Government had other ideas, feeling that cannabis, rather than being handled by a proposed new specialist regulator, independent of the established TGA framework, should instead be subject to the rigid system of testing, registering and oversight like any other drug, based largely on the pharmaceutical model.

One of its main concerns, it turned out, was that the bill might contravene Australia's international treaty obligations under the United Nations 1961 Single Convention on Narcotic Drugs.[2] This document places the same restrictions on the cannabis plant as it does on cocaine, heroin and other opiates – an important point given Australia cultivates well over half the world's poppies used to make prescription opioid medicines. This is a lucrative industry the government doesn't wish to see jeopardised, though inclusion of cannabis within the Single Convention is today widely criticised as policy that fails to keep pace with science.

> "If you would understand anything, observe its beginning and its development"
>
> **- Aristotle (385-325 BCE)**

This is evident given the plant's main psychoactive ingredient, delta-9 tetrahydrocannabinol (THC), wasn't structurally identified until 1964[3] (three years after the Single Convention came into being), therefore its inclusion was based on no established toxicological or pharmacological understanding of the plant whatsoever. Hardly the poster child for the application of evidence-based science in helping guide policy decisions.

In any case, responsibility for cannabis was in the end handed to existing departments and processes within government in a completely divergent initiative and on 24 February 2016 (the anniversary of Dan Haslam's death), the Australian Government passed the Narcotic Drugs Amendment Bill.

The legislation received overwhelming cross-bench support, going through parliament in record time. It amended the old Narcotic Drugs Act of 1967 to allow the cultivation, research and manufacturing of cannabis and cannabis based products in Australia for the first time in over 50 years. Labor had initially wanted to place this Bill, like its predecessor, before a committee for further review. Instead, it agreed to forego such a process on the proviso an advisory council would be established to assist in the writing of the accompanying regulations, but the government reneged on its pledge. Not only did the promised 'Australian Advisory Council on the Medicinal use of Cannabis' fail to contribute to any of these important foundational regulations, it wasn't even formed until January 2017, months after the rules took effect on 1 November 2016.

Other changes necessary for the Narcotic Drugs Amendment Bill to function were needed as well, so in August 2016 'cannabis' (i.e. the plant, its resins, seeds and extracts) as well as certain isolated cannabinoids such as THC, were reclassified in the Standard for Uniform Scheduling of Medicines and Poisons (SUSMP) - the Poisons Standard from a Schedule 9 'Prohibited Substance' to a 'Controlled Drug' (Schedule 8). Cannabidiol (CBD), the cannabinoid which exhibits significant anti-convulsant properties currently being investigated in epilepsy trials, was placed in Schedule 4 ('Prescription Only Medicine').

As a result of this bill, MC cultivation, manufacturing and research licensing now came under the jurisdiction of the Office of Drug Control (ODC) – part of the Department's Health Products Regulation Group. The ODC enforces very strict requirements in regards to security, risk of diversion, chain of custody and transport of MC products amongst numerous other duties, and works in tandem with its sibling, the TGA. This latter government department is responsible for not only patient access to MC, but also MC finished product requirements for safety, efficacy and quality like any other pharmaceutical medication – a process which is not only time consuming, but incredibly expensive.

Critics of the scheme, such as businessman and philanthropist Barry Lambert (who donated $34 million for MC research to Sydney University), condemned the ODC/TGA regulations as being too restrictive and has taken his hemp business and research dollars to the United States.

Patient access too is now a lengthy and protracted process, with the TGA's Special Access Scheme (SAS) 'Category B' and the Authorised Prescriber scheme being the only ways patients can get hold of the drug legally. And to make matters worse, in a behind-closed-doors move, ministers tweaked the SAS so that the other category within it – 'Category A'[4] designed for the terminally ill – was not applicable for cannabis after the regulations came into effect.

This means that the one patient group most in need on compassionate grounds is being made to wait longer periods of time for a successful

'Category B' application. Time, which many of them simply do not have. At the time of writing this article, another lobby group (i.e. Medicinal Cannabis Advisory Group – Queensland) is petitioning MPs to disallow this regulation, but their success looks a long way from certain.

A further problem with the access schemes is that its gatekeepers – the medical practitioners who have to authorise and make applications for their patients – have no training in the use of MC and know little of the intricacies of the endocannabinoid system; the array of receptors around the body responsive to the plant's chemicals. Doctors are therefore reluctant to open themselves up to potential litigation for prescribing something they don't understand (not an unreasonable position if your career could be on the line). So when the government blanketed the media, declaring doctors could now prescribe cannabis, it was nothing more than lip service and provided the medical profession as a potential scapegoat for lack of uptake of the MC program by patients.

On top of this, not only are the ODC and TGA involved in MC Regulations, but the individual State and Territory Governments also have a say in how cannabis is used within their own jurisdictions. Everything the original Regulator of Medicinal Cannabis Bill 2014 identified as being an obstacle to patient access has come to pass, and two Federal Government agencies along with individual State and Territory requirements are now involved in the process. Patients and their doctors are drowning in a labyrinth of documentation and legal preconditions, diverting many back to black market products – the very thing the regulations were designed to put a stop to.

Recent police raids on compassionate MC suppliers, such as Jenny Hallam in South Australia, have now left hundreds of patients without what is for some a life-saving medicine. One has to question who will be held legally responsible should patients die or suffer catastrophic seizures because their medication was confiscated – regardless of its legal status?

Where are we now?

Perhaps this is best summarised by Lucy Haslam herself, who's been tirelessly campaigning since the start:

"*Initially I felt immense pride that Australian leaders saw fit to pass legislation on the basis of compassion for the sick, but what followed was a complete travesty. The Government failed to appoint an Advisory Council and set barricades and brick walls before genuine patients in distress. One can only conclude this was done wilfully to prevent patient access.*"

As I write this on 23 February 2017, I am aware of only one cultivation licence that has been issued by the ODC to an Australian company. Recent changes announced by the Federal government to import MC products for patients until an Australian supply is established are welcome and should reduce the wait time on accessing product, but do nothing to speed up or simplify the patient application process to access the MC in the first instance.

Whilst regulating something as complex as the cannabis plant certainly has its own unique challenges and will no doubt continue to evolve as time goes on, we can hope that people are put before politics and profits. Let us finish with another quote, this time from Cicero – a timely reminder to those who have it within their power to change the current state of affairs.

Salus populi suprema lex esto, which translates as – "Let the welfare of the people be the supreme law" – Cicero (106-43 BC).

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Disclosure:
The Author currently sits on the Scientific Advisory Boards for both BioCeuticals and United in Compassion.

Pyrrole disorder: identification and treatment

Belinda Fay, BSc ND (Adv.)

Originally identified in the 1950s by Dr Abram Hoffer, Dr Humphrey Osmond and Dr Carl Pfeiffer, pyrrole disorder, or pyroluria, refers to a condition that results in an overproduction of pyrroles or hydroxyhaemopyrrolin-2-one (HPL). HPL is a by-product of haemoglobin (Hb) synthesis and the disorder reflects an abnormality in the synthesis and metabolism of Hb.[1-3]

Most individuals have low levels of pyrroles at any given time, but pyrrole disorder is identified by an unusually elevated level of pyrroles in the urine.[1,2] Most people have less than 10mcg/dL of HPL in their urine. The upper limit of normal for HPL varies between 8-20 mcg/dL and levels greater than 20 mcg/dL are considered to be positive for pyrrole disorder.[1,4]

Pyrrole disorder is also known by the name 'Mauve Factor' due to the purple appearance of pyrroles in urine chromatograms stained with Ehrlich's reagent.[5]

It was through Hoffer's interest in the possible biochemical aetiology of schizophrenia that HPL was discovered. Elevated HPL has been documented in many cognitive, affective, and neurobehavioural disorders and is linked to the following conditions:[3,4]

- Down's syndrome
- bipolar disorder
- anxiety
- depression
- autism
- epilepsy
- learning disabilities
- ADHD
- neuroses
- alcoholism.

Who does it affect?

Pyrrole disorder affects up to 10% of the population, and the incidence can increase to 18-35% in people with psychological disturbances, learning or behavioural problems. Children with behavioural issues, ADHD and autism have been found to have pyrrole disorder in association with high levels of oxidative stress.[6,7]

Although HPL concentrations tend to be high in patients with mental illness, elevated levels of HPL are not specific to these patients.

Subjects with elevated histamine levels may also have elevated HPL, indicating an allergy component to the condition.[5]

Pyrrole disorder should be considered in patients who may not respond to medications such as SSRIs and antipsychotics but show improvement with nutritional therapy.[8]

Genetic basis

There is evidence that pyrrole disorder is a genetic condition. If one parent has pyrrole disorder then there is a 50% chance that it may be passed onto a child. If both parents are affected then there is a 75% chance of inheriting the disorder.[1] Even if just one family member is affected it is recommended that familial genetic testing be investigated. [9]

Epigenetic vulnerability is associated with pyrrole disorder.[1] The severity of the condition is impacted by stress and may also be triggered by a traumatic event.[8]

Symptoms manifest as vitamin B6 and zinc deficiency

HPL binds several nutrient cofactors, in particular vitamin B6 and zinc, essentially rendering them unavailable for use by the body.[2,4] B6 and zinc are critical for digestion, immune function, cognition and emotion, and chronic depletion can have serious consequences on wellbeing. The signs and symptoms of pyrrole disorder correlate with a deficiency of B6 and zinc.[3]

A combination of physical, emotional and cognitive symptoms as well as stress are associated with pyroluria,[5] so it is important to consider that not everyone that exhibits these symptoms will have pyrrole disorder, and not everyone with the disorder will have all of the symptoms.[1-3] Some of the symptoms of pyrrole disorder may include:

- poor dream recall
- mid morning nausea
- poor morning appetite
- white spots on nails
- stretch marks
- pale complexion
- digestive complaints
- joint and/or skin complaints
- anxiety
- mood swings
- sensitivity to noise and lights
- histrionic (dramatic).[1-3]

Nutrients including biotin, magnesium and manganese are also altered in this condition due to their intricate association with B6 and zinc and their biochemical roles in metabolism and neurotransmission.

Altered haem production

The breakdown of haem is fundamental to the mechanisms for HPL formation and accumulation in the body.[5] Depression of haem lowers zinc, B6 and biotin, increases nitric oxide and antioxidant leak from mitochondria and augments oxidative damage to cells.[4,7] As a marker for B6 and zinc deficiency, HPL is also a potential biomarker for oxidative stress.[2-4,6]

Neuronal metabolic activity is dependent on haem, and depression of haem leads to metabolic crisis that negatively affects mitochondria and neurons. The corresponding depletion of B6, zinc and magnesium results in elevated levels of oxidative and neural toxicity and depleted production of calming neurotransmitters such as GABA and serotonin.[2,4]

Elevated HPL has been linked to digestive disorders.[3] Imbalance in gut flora may alter haem biosynthesis and a relationship exists between elevated pyrrole levels and elevations in indicans and urobilinogens.[5]

Stress and oxidative damage negatively affect intestinal permeability, and intestinal permeability in turn increases the absorption of HPL.[3,5]

Pyrrole disorder and mood

In pyrrole disorder the inhibitory neurotransmitters GABA and serotonin are depleted, and excitatory neurotransmitters dopamine and noradrenaline are imbalanced.[7,10] When there is an imbalance in the equilibrium between inhibitory and excitatory neurotransmitters, mood disorders such as depression and anxiety evolve.

GABA dampens nerve activity in the brain leading to feelings of calm and relaxation. As the main inhibitory neurotransmitter, GABA modulates anxiety. **Serotonin** controls mood, appetite and sleep. Individuals with depression often have lower levels of serotonin. Imbalance in **dopamine** levels have been linked to schizophrenia and ADHD. Dopamine influences motivation and plays a role in one's perception of reality. Involved in the brain's reward system dopamine is also thought to play a role in substance abuse.
Norepinephrine can trigger anxiety and is involved in some types of depression.[11,12]

Deficiencies in nutrients including B6, zinc and polyunsaturated fatty acids (PUFAs) are linked to mood disorders as these nutrients play an important role in neurotransmitter and neurologic function.[2]

P5P and mood

Pyridoxal-5-phosphate (P5P) is the metabolically active, phosphorylated form of vitamin B6 and is a coenzyme for the biosynthesis of GABA, dopamine, norepinephrine and serotonin. Vitamin B6 concentrations are significantly higher in the brain than blood levels hence B6 deficiency has pronounced neurologic effects.[13] P5P protects neurons from oxidative stress, possibly by increasing energy production and lowering excitotoxicity.[4]

Zinc and mood

Zinc has catalytic, structural and regulatory roles in cellular metabolism in the brain. It has a role in neurotransmission mediated by glutamate and GABA.[13] There is also growing evidence that major depressive disorders are associated with reduced serum levels of zinc.[14] Anxiety is further aggravated if copper levels are elevated due to zinc deficiency.

Treatment of pyrrole disorder

Combined with a wholistic nutritional approach, correct diagnosis of pyrrole disorder is critical to successful management of the condition. Long term supplementation of B6 and zinc is necessary for ongoing suppression of HPL and associated symptoms.[4]

Vitamin B6 (200-800mg daily) in combination with zinc (25-100mg daily) has been shown to suppress HPL and achieve an optimal symptomatic response (optimal initial doses may be higher than maintenance doses). Higher urinary HPL may require a proportionately higher dosing of B6 and zinc. Measurements of HPL at regular intervals will help to determine maintenance dosages of these nutrients on an individual basis.[4,9]

Primary determinants of B6 dosing are clinical symptoms and the suppression of HPL. Useful signs include poor recall of dreams or morning nausea and/or anorexia.[9]

Periodic testing of a patient's zinc levels is recommended to monitor zinc to copper ratio. Taking 50mg/day or more of supplemental zinc over a period of time can interfere with the bioavailability of copper as high zinc intake induces the intestinal synthesis of metallothionein, a copper binding protein.[9,15]

Intestinal permeability

Pyrrole disorder may manifest as a result of poor diet and/or digestive issues contributing to depletion of essential nutrients. Intestinal permeability should be considered when a patient presents with elevated HPL.[7] A multistrain probiotic and nutrients to support intestinal permeability including zinc will facilitate appetite and improve nutrient assimilation.[16]

Manage stress

Stress management is crucial for these patients as is supporting adrenal health. Increased HPL excretion is classically associated with emotional stress, which is also associated with oxidative stress.[9] Adrenal support could include the use of adaptogenic herbs such as withania and ginsengs.

Prolonged physical or emotional stress elevates adrenaline and cortisol and these both interfere with serotonin. Low serotonin can also exacerbate sugar cravings.[17]

Nutritional considerations

Magnesium is important for normal brain function and deficiency results in both neurologic and muscular symptoms. Habitual inadequate intake of magnesium may also result in a chronic state of inflammation, which can potentially amplify depressive symptoms. High doses of zinc in supplemental form may interfere with magnesium absorption, so supplementation of these minerals should be staggered.[13,18,19]

Manganese is involved in the conversion of glutamate to glutamine in the brain. Glutamate is an excitotoxic neurotransmitter and a precursor to GABA, an inhibitory neurotransmitter.[20] Suppression of manganese may result from excessive zinc supplementation.[9]

Biotin is involved in the metabolism of fatty acids and amino acids and a deficiency contributes to neurologic symptoms including depression.[13]

Vitamin C accumulates in the central nervous system, particularly in the neurons. It is required for the conversion of dopamine to norepinephrine, and prevents oxidative damage to the lipids and proteins in the brain.[13]

Glutathione (GSH) is the ubiquitous intracellular antioxidant. Plasma levels of reduced GSH are decreased in diseases associated with greater oxidative stress.[4]

Essential fatty acids are essential to normal brain and behavioural function. Elevated HPL depletes gamma linolenic acid (GLA) alongside zinc, B6 and magnesium which are required for EFA conversion in the body.[2,9,21]

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Dietary recommendations

- Include a rainbow of varied vegetables to improve antioxidant status.
- Limit inflammatory foods that may increase gut permeability.
- Increase zinc rich foods e.g. red meat, oysters, nuts and legumes, eggs.
- Include magnesium rich foods to offset high dose zinc e.g. green leafy vegetables, wholegrains, nuts.
- Take care with grains and cereals as they potentially bind with zinc (consider staggered supplementation away from grain/cereal consumption).
- Avoid food sources and nutritional supplements containing copper and red/yellow food dyes.[22]

Neuroinflammation in mood disorders and cognitive decline

Petra Hunter, ND BHSc Nat

Under normal circumstances inflammation is a natural, protective immune response to injury, infections, and oxidative stress that serves to facilitate healing. Yet, if left uncontrolled, inflammation can cause severe damage throughout the body, including in the central nervous system.

Inflammation is regulated by a range of mediators, including cytokines, which can be either pro-inflammatory, such as the interleukins 1 (IL-1), 2 (IL-2) and 6 (IL-6), tumour necrosis factor alpha (TNF-alpha), and interferon gamma (IFN- gamma), or anti-inflammatory, for example IL-4, IL-5 and IL-10.[1,2] Cytokines, together with a few selected inflammatory markers, such as C-reactive protein (CRP), are clinically used as biomarkers for inflammatory disease.

The role of altered cytokine profiles in psychiatric disorders, such as cognitive decline and depression, is supported in several lines of evidence.[2]

Inflammation and cognitive decline

Ageing is naturally associated with decreases in cognitive function and a growing body of evidence suggests that age-related inflammation may contribute to these changes.[3] Only one in 1000 older adults exhibit no evidence of cognitive deterioration.[4]

While research has been conflicting regarding which inflammatory markers are most predictive of cognitive decline, findings have been generally consistent that overall inflammation and immune function are closely tied to cognitive function and may contribute to increased risk of cognitive decline and dementia.[4]

In a longitudinal examination of inflammatory markers and global cognitive decline, participants in the highest tertile of IL-6 or CRP serum concentrations performed significantly worse at baseline and follow-up testing, with a 24% increased risk of cognitive decline over a two year period in comparison to those participants in the lowest tertile.[4] A significant inverse relationship between executive function and visuospatial ability has also been related to serum CRP levels.[4]

Moreover, researchers have demonstrated that older adults with lower levels of IL-6 and CRP are more likely to maintain their baseline levels of cognitive function (as opposed to decline) over an eight year follow-up period.[5]

Oxidation, inflammation, and Nrf2

Like inflammation, oxidative stress has been increasingly recognised as a contributing factor in ageing and in various forms of pathophysiology generally associated with ageing.[6]

Transcription factor Nrf2 (nuclear factor erythroid 2-related factor 2) plays a central role in the induction of cytoprotective genes in response to oxidative stress.[7] Once activated, Nrf2 becomes a part of the Antioxidant Response Element (ARE) which is the master regulator of the antioxidant response. Nrf2 modulates the expression of hundreds of genes, including antioxidant enzymes (such as glutathione and superoxide dismutase) and phase 2 detoxification enzymes, as well as genes that control disparate processes such as immune and inflammatory responses.[6,8] Thus, the Nrf2-mediated signalling pathway provides a pivotal line of defence to counteract environmental insults and endogenous stressors.[8]

A study on institutionalised older adults demonstrated pronounced oxidative stress, reduced antioxidant status, and high levels of pro-inflammatory cytokines. The elevated levels of inflammatory markers were correlated with increased oxidative stress, and both were associated with low cognitive performance.[9]

Many studies have shown Nrf2 to be a promising target for the prevention of chronic inflammatory disorders, including cardiovascular disease, neurodegenerative diseases and carcinogenesis.[8]

Who is at risk?

Given the strong association between cognitive decline and inflammation, it is important to identify those patients who are at increased risk of inflammation. While elevated inflammatory profiles occur with ageing even in the absence of disease, there are several factors that may increase inflammation levels beyond senescence.[4]

For example, those with metabolic syndrome, diabetes, or obesity, are at heightened risk for innate and chronic inflammation.[4] Lifestyle factors such as poor diet, lack of physical exercise, inadequate sleep, and smoking can also increase systemic inflammation.

An inflammatory dietary pattern characterised by higher intake of red meat, processed meat, peas and legumes, and fried foods, and lower intake of wholegrains correlates with elevated IL-6 levels. Researchers who followed more than 5000 participants between years 1991-2009 found that inflammatory eating habits are linked with faster cognitive decline after multivariable adjustment.[10]

Other research shows that obesity and high fat feeding leads to systemic inflammation and is associated with a range of comorbidities, including cognitive dysfunction.[11] Greater body mass has been indirectly associated with declines in memory and executive functioning via elevated levels of CRP.[12]

Psychological stress is another important risk factor for cognitive loss. Stress can activate the immune response via the hypothalamic-pituitary-adrenal (HPA) axis, leading to the release of the stress hormone cortisol. High levels of cortisol may lead to memory deficits in healthy older adults.[4] The pro-inflammatory cytokines IL-1 and TNF-alpha also stimulate the HPA axis, further contributing to stress-induced cognitive decline. Thus, it appears feasible that inflammation may mediate the effects of stress on cognitive function.[4]

Psychological distress is also linked to inflammation. Findings from studies suggest that depressive symptoms are associated with increased pro-inflammatory cytokine profiles and that the level of cytokines corresponds to the severity of symptoms.[4] Depression may also adversely influence cognitive function by affecting working memory, executive function, and processing speed.[4]

Inflammation in mood disorders and depression

Patients with major depressive disorder (MDD) exhibit all of the fundamental features of an inflammatory response, including increased expression of pro-inflammatory cytokines.[13]

Meta-analyses of the literature suggest that peripheral blood IL-1 beta, IL-6, TNF-alpha and CRP are the most reliable biomarkers of increased inflammation in patients with anxiety and depression.[13,14]

Other factors that support the role of inflammation in depression include:[15]

- a large percentage of individuals with inflammatory illnesses struggle with depression
- elevated inflammatory markers are associated with MDD
- pro-inflammatory cytokines initiate a cascade of reactions that lower serotonin levels (via activation of the extrahepatic enzyme IDO, which degrades tryptophan, a precursor to serotonin)
- anti-inflammatory agents such as cyclooxygenase-2 (COX-2) inhibitors, aspirin, and TNF receptor antagonists can enhance depression treatments
- blockade of cytokines, such as TNF, or inflammatory pathway components, such as COX-2, has been shown to reduce depressive symptoms in patients with rheumatoid arthritis, psoriasis, cancer and MDD
- inhibition of inflammatory pathways can improve mood.[14]

There also appears to exist a relationship between inflammation and treatment-resistant depression (TRD), which occurs in about one third of patients.[14] Those who do not respond to standard antidepressant therapy tend to show an increased level of inflammatory markers.

Patients with other neuropsychiatric disorders, including anxiety and schizophrenia, also present with elevated markers of inflammation.[13]

Curcumin

Curcumin is derived from the rhizome of *Curcuma longa* (turmeric), a member of the ginger family. Curcumin is known to exhibit various therapeutic properties, including antioxidant and anti-inflammatory, which suggest a potential neuroprotective nature of this compound.

The protective activity of curcumin may be mediated via several mechanisms, including:[16,17]

- modulation of pro-inflammatory cytokines, including TNF-alpha, IL-1 and IL-6
- inhibition of nuclear factor-kappa B (NF-kB), a major regulator of inflammatory mediators
- inhibition of lipoxygenase (LOX), COX-2, and iNOS expression, leading to decreased levels of prostaglandin E2 (PGE2) and nitric oxide
- induction of phase 2 antioxidant enzymes via activation of Nrf2 signalling.[18]

Curcumin has been shown to exhibit activity against various neurological diseases, including age-associated neurodegeneration and depression, as well as Alzheimer's disease, multiple sclerosis, schizophrenia, neuropathic pain, and cerebral injury.[16]

Even though clinical data is limited, epidemiological evidence from curcumin-consuming populations such as India shows that long term consumption of curcumin is slinked with a remarkably lower incidence rate of neurodegenerative cases.[19]

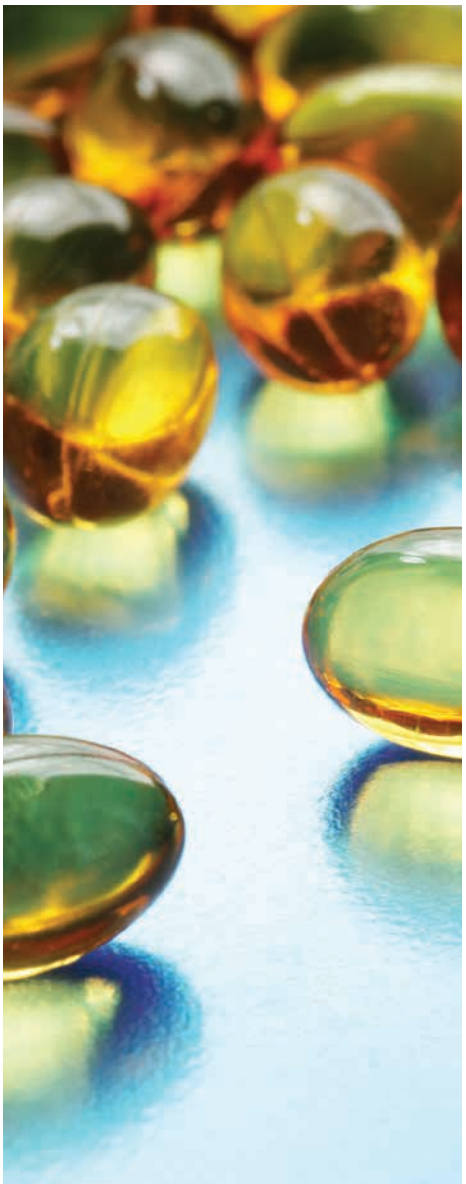
Omega-3 fatty acids (krill and fish oils)

The healthy brain is highly enriched with the long-chain omega-3 fatty acids eicosapentaenoic acid (EPA) and docosahexaenoic acid (DHA) and their derivatives, which serve to regulate several biochemical processes, including cell survival, neurotransmission, cell survival and neuroinflammation.[20]

Omega-3 fatty acids may provide a range of neurobiological activities via modulation of neurotransmitters, inflammation, oxidation and neuroplasticity.[20] A body of evidence has implicated dietary deficiency in EPA/DHA in the aetiology and pathophysiology of numerous psychiatric disorders.

The anti-inflammatory effects of omega-3 fatty acids include:

- Inhibitory effects on arachidonic acid (AA) metabolism (competitive inhibition of COX and LOX favours the synthesis of anti-inflammatory prostaglandins (PGE3) and leukotrienes (LTB5) rather than their pro-inflammatory counterparts PGE2 and LTB4).[21]
- Inhibitory effect on NFkB activation and pro-inflammatory cytokines, including TNF-alpha, IL-1beta, IL-6.[21]
- Decreased CRP.[22]



Omega-3 fatty acids in mood disorders

The antidepressant effect of fatty acids has been reported in a number of clinical trials. Insufficient DHA is associated with dysfunctional neuronal membrane stability and transmission of serotonin, noradrenalin and dopamine, which may contribute to the aetiology of mood and cognitive dysfunction of depression.[23] In addition, the omega-3 fatty acids may be used as an adjunct to enhance the efficacy of standard treatment.

When omega-3 fatty acids were administered as a combination therapy with citalopram, a significantly greater improvement in Hamilton Depression Rating scale score was noted, suggesting that there may be an advantage to combining omega-3 fatty acids with a selective serotonin uptake inhibitors in the treatment of individuals with MDD.[24]

Another study comparing the therapeutic effects of EPA (1000mg/day), fluoxetine and a combination of both in MDD, found that the combination was significantly better than either therapy alone. Interestingly, when taken alone, fluoxetine and EPA were similarly effective in controlling depressive symptoms; response rates were 50%, 56% and 81% in the fluoxetine, EPA and combination groups, respectively.[25]

Omega-3 fatty acids support cognitive function

Higher intakes of essential fatty acids have been found beneficial for the ageing brain and may provide a novel strategy to maintain cognitive function into old age.[26-28]

It has been suggested that krill oil may be a superior source of omega-3 fatty acids in this cohort as its fatty acids are incorporated into phospholipids, leading to enhanced absorption and bioavailability, rather than fish oil in which the omega-3's are present as triglycerides.[28]

However the difference in effect on cognitive function between phospholipid and triglyceride omega-3 storage has not been elucidated.[28]

Improved cognitive performance has also been reported in healthy adults following supplementation with DHA,[29] and a higher Omega-3 Index score has been associated with better information processing speeds and fewer errors of omission in healthy adolescent students.[30] In children, increases in erythrocyte omega-3 fatty acids, specifically DHA, may improve literacy and behaviour in those with attention deficit hyperactivity disorder.[31]

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Probiotics: an integrative approach for depression and anxiety

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Our microbiota is a complex community of organisms working together to maintain dynamic ecological balance. Of the trillions of bacteria that inhabit the human body, 80% live in the gut.[1] These bacteria are not only essential for normal GI function, but also for systemic processes, brain development and function, behaviour, and cognitive and emotional processing.

This one kilogram mass of bacteria may weigh the same as the brain, yet the gut microbiota is far superior in genomic and biochemical complexity.[2] Its ability to communicate with the brain and nervous system through a network called the gut-brain axis is not yet fully understood, but with a large research focus in this area new insights are rapidly developing.[1]

'The emerging links between our gut microbiome and the central nervous system (CNS) are regarded as a paradigm shift in neuroscience with possible implications for not only understanding the pathophysiology of stress related psychiatric disorders, but also their treatment.'[3]

The gut-brain axis: a bidirectional pathway

The gut-brain axis was first discovered in an animal study in 2004, when, during an increased hypothalamic-pituitary-adrenal (HPA) stress response, the levels of brain-derived neurotrophic factor (BDNF) in the hippocampus decreased.[4] BDNF influences survival and differentiation of neurons, formation of functional synapses and brain neuroplasticity.[5] Since then, both experimental and human clinical trials have shown the gut-brain axis to be a bidirectional network involving complex signalling pathways.[2,4,6] This network is comprised of:[1,6]

- gut microbiota and its metabolites
- CNS
- enteric nervous system (ENS)
- the parasympathetic and sympathetic branches of the autonomic nervous system (ANS)
- neuroendocrine and neuroimmune pathways.

Communication between the gut microbiota and the nervous system occurs through afferent and efferent nerve pathways with five recognised routes, all of which may be involved in the regulation of emotion and behaviour:[1,6]

1. neuroanatomical network of the gut brain axis (through the vagus nerve, ANS and gut ENS)
2. neuroendocrine-HPA axis pathway
3. gut immune system (involving toll-like receptors [TLRs] and cytokines)
4. neurotransmitters and neural regulators, such as short chain fatty acids (SCFAs), made by gut bacteria
5. intestinal mucosal barrier and blood-brain barrier.

It is important to remember that this complex axis works bidirectionally and mutually. Studies show that an altered emotional state and chronic stress can adversely affect gut microbiota composition and function. In turn, this may lead to increased intestinal permeability, allowing greater access of bacteria, metabolic products, such as lipopolysaccharides (LPS) and neuroactive peptides to enter the circulation and affect areas of the nervous system that regulate cognition, mood and behaviour.[7] Additionally, an imbalance of bacteria in the gut can alter immune and inflammatory responses leading to vagal nerve activation and changes to brain and neural functions, as well as further damage to the intestinal barrier.[7] A dysfunction in either gut or brain has potential health effects on the body as a whole.[8]

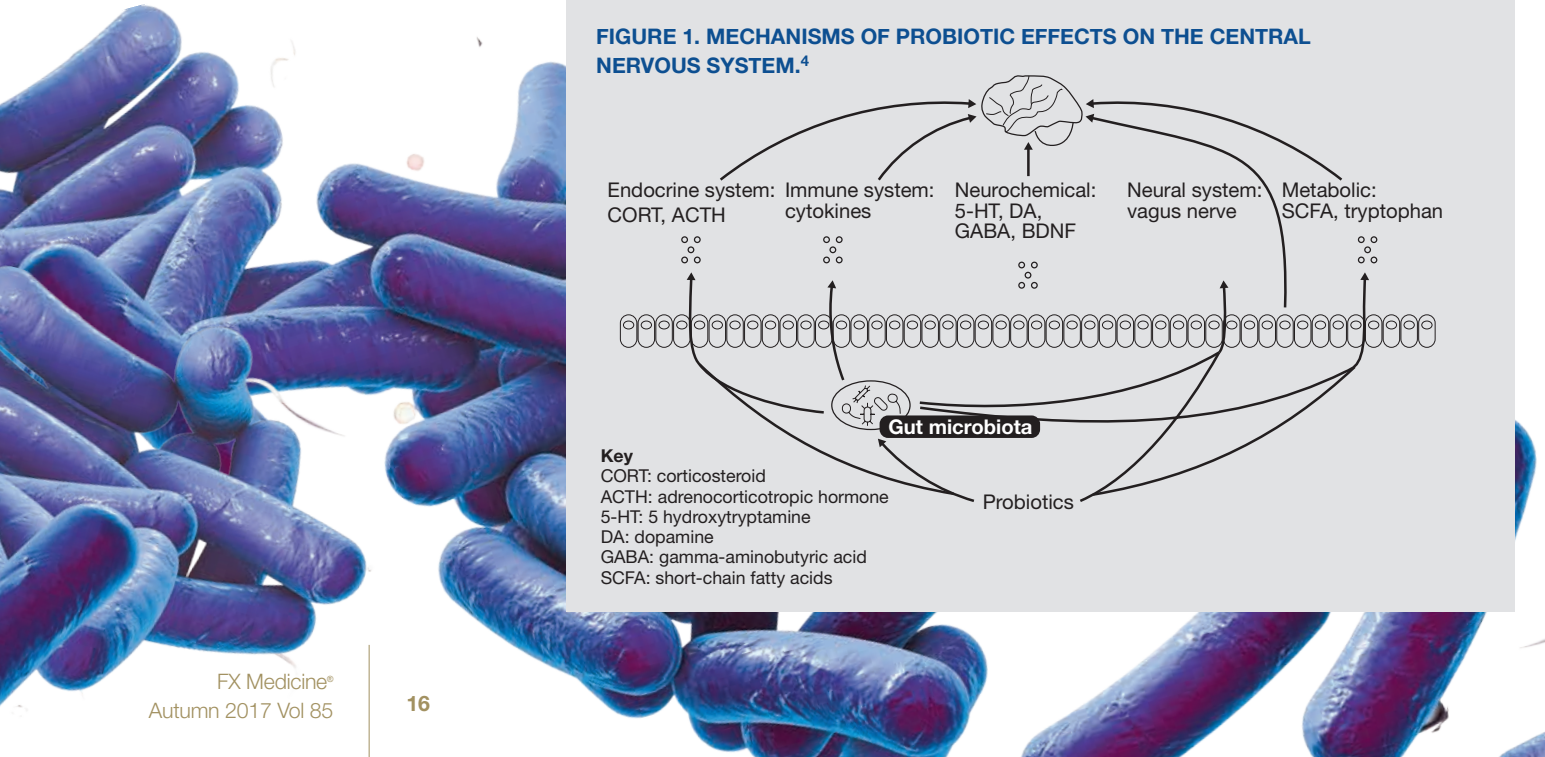

FIGURE 1. MECHANISMS OF PROBIOTIC EFFECTS ON THE CENTRAL NERVOUS SYSTEM.[4]

Key
CORT: corticosteroid
ACTH: adrenocorticotropic hormone
5-HT: 5 hydroxytryptamine
DA: dopamine
GABA: gamma-aminobutyric acid
SCFA: short-chain fatty acids

The importance of probiotics

During adult life the core composition of the gut microbiota remains fairly stable; however, lifestyle, stress, drugs, infection and genetic influences may change the microbiota and its genome (collectively called the microbiome), leading to wide ranging health effects.[1,6] Therefore, the use of probiotics may be necessary, with studies showing they can beneficially alter the gut environment and microbiota composition, reduce inflammation, strengthen the intestinal barrier, modulate the HPA axis, produce key neurotransmitters, such as GABA and serotonin, and generate SCFAs and a biologically active form of catecholamines. They also have the ability to regulate circulating levels of the precursor to serotonin – tryptophan, directly influencing serotonin's production.[2,4,6,8] All of these actions have an impact on gut and brain functionality.

Targeted probiotic strains in stress, anxiety and depression

Preclinical and clinical research shows two specific strains of probiotics, *Lactobacillus helveticus* R0052 and *Bifidobacterium longum* R0175, may be used beneficially for improving the physical and psychological symptoms and development of stress and mood disorders, such as anxiety and depression.

In a 2008 double-blind placebo-controlled trial, this probiotic combination significantly improved the stress induced gastrointestinal symptoms of nausea, vomiting and abdominal pain in healthy but chronically stressed individuals. The total dose given was 3 billion colony-forming units (CFU) per day for three weeks.[9]

Following on from this positive result the same researchers tested this probiotic combination and dose in a longer trial of 30 days, and included a range of psychological questionnaires and urinary free cortisol testing.

TABLE 1. MAIN PRINCIPAL MECHANISMS OF THE BIDIRECTIONAL BRAIN-GUT-MICROBIOTA AXIS

From gut microbiota to brain:
• Production, expression and turnover of neurotransmitters (i.e. serotonin, GABA) and BDNF
• Regulation of intestinal barrier and tight junction integrity
• Modulation of enteric sensory afferents
• Bacterial metabolites
• Mucosal immune regualtion
From brain to gut microbiota:
• Alteration in mucus and biofilm production
• Alteration in motility
• Alterations of intestinal permeability
• Alteration in immune function

Compared to placebo, there was a statistically significant reduction in anxiety and depression, with reduced markers of psychological distress, including somatisation, anger and hostility.

Additionally, median free cortisol levels decreased in those taking the probiotics. This is significant as cortisol regulation is often impaired in chronic stress and suggests that these probiotics moderated the HPA axis response to stress.[10] To test how this combination would work in those with low stress levels, the researchers performed a secondary analysis only looking at the subjects who had low cortisol levels at the start of the study. They found the results were the same except there was a greater benefit for those with obsessive compulsiveness, anxiety, paranoid ideation and heightened perceived stress.[11]

In these clinical trials the probiotic combination was found to be safe, well-tolerated, no reported adverse reactions, and did not demonstrate any addictive or rewarding properties or cause any learning or memory deficits, often seen with pharmaceuticals used in these conditions.[9,11] Preclinical studies have also supported the use of these probiotics, indicating they may protect neural networks, restore negative HPA axis feedback, modulate ANS responses to stress, reduce proinflammatory cytokines, and benefit intestinal barrier stability and brain plasticity, all of which can assist in alleviating stress and mood disorders.[12,13]

Supportive probiotics

A recent study has shown the benefits of the probiotic species *L. acidophilus*, *L. casei* and *B. bifidum*, to significantly reduce depression scores in major depressive disorder (MDD), while increasing levels of the antioxidant glutathione and decreasing serum insulin levels.[14] Even in non-depressed individuals, *B. bifidum*, *B. lactis*, *L. acidophilus*, *L. brevis*, *L. casei*, *L. salivarius* and *Lactococcus lactis* reduced overall cognitive reactivity and negative thoughts associated with sad mood in another study.[15] Other probiotic strains, without specific studies on their beneficial use for brain health, can be used to restore and maintain gut health and thereby support the gut-brain axis. *B. lactis* HN019 has shown significant improvement in gut transit time and supports microbiota levels.[16,17] This strain, along with *L. rhamnosus* HN001, has also had positive effects on cellular immunity.[18] Immune health, and therefore appropriate inflammatory response, is important for the gut-brain axis communication and function of both systems.

Psychobiotics for the gut-brain axis

A healthy and diverse gut microbiota is crucial. Dysbiosis, especially at the early and late stages in life, can have a profound impact on brain function from a neurological and mental health perspective.[2,7] Emerging evidence continues to examine the role of the gut-brain axis, with studies revealing probiotics may work as potential psychobiotics, due to their ability to be beneficial for mental health.[2] This increases our understanding of the brain and its relationship with the gut, and provides more integrative and potentially effective treatment options for neuropsychiatric conditions, such as depression and anxiety.[1]

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Herbal mechanisms of action on the immune system

Georgia Marrion, BHSc(Comp med) AdvDipHSc(Nat) MHumNut

Herbal substances such as *Echinacea purpurea*, *Andrographis paniculata*, *Astragalus membranaceous*, *Inula helenium*, *Olea europaea*, *Sambucus nigra* and *Thymus vulgaris* are often used to support immunity. Just like the complexity of the immune system, the specific mechanisms of action of these herbs on immune activity is heterogeneous and complex.

The immune system is significantly complex in its physiology and functionality. Maintaining homeostasis involves an intricate interaction between the innate and adaptive immune systems and the cells, receptors, molecules and chemical substances that comprise these systems.[1-3]

This complexity also extends to the impact of many factors on immune function, including diet and nutritional status, lifestyle, age, medications, stress, microbiome composition, and physiological and genetic variability.[4-8]

Echinacea purpurea (echinacea)

Echinacea purpurea is commonly used for the amelioration of upper respiratory tract infections (URTI), cold and flu symptoms and overall immune system support, and is perhaps the herb most commonly associated with improvement of immunity.[9]

It has been used in traditional medicine for many health concerns including wound healing, throat and yeast infections and coughs,[10,11] and overall the clinical evidence indicates it is beneficial for the treatment of cold, flu and URTI symptoms as well as urinary tract infections via immune stimulation and modulation.[9-11]

The primary active constituents isolated from the aerial parts and roots includes the caffeic acid derivative cichoric acid (2,3-odicaffeoyl-tartaric acid), alkamides, volatile oils, polysaccharides and melanins, and these constituents are responsible for the herb's impact on immunity.[9-13]

E. purpurea influences both innate and adaptive immune activity via a number of mechanisms including promoting white blood cell (leukocyte, monocyte, lymphocyte) production, activation and mobility, stimulating phagocytic activity, and cytokine synthesis in granulocytes and macrophages (tumour necrosis factor alpha [TNF-alpha], interleukins 1, 6, 8 and 10, interferon),[9-11] as well as modulating regulatory T-cells number and function,[14,15] and dendritic cell differentiation and expression.[16,17]

Other mechanisms include inhibiting viral receptor binding capacity and pro-inflammatory compounds (COX-1, COX-II, NF-kB).[10,18]

Andrographis paniculata (andrographis)

The aerial parts of *A. paniculata* have been used extensively in traditional Ayurvedic and Chinese medicine systems for a range of conditions including URTI symptoms, sinusitis, bronchitis and tonsillitis, pneumonia, whooping cough and urinary tract infections.[19,20,22]

The active constituent that is considered to be the most biologically significant for its immune modulatory and anti-inflammatory activity is the diterpene lactone andrographolide.[19-22] Human clinical evidence demonstrates that *A. paniculata* is beneficial for the alleviation of URTI symptom severity and frequency.[20,23,24]

Animal and *in vitro* data has found that there are many underlying mechanisms that contribute to these therapeutic effects.

These include stimulation of innate immunity via macrophage phagocytosis and lymphocyte production and activity,[20-22] and adaptive immunity by induction of antibody synthesis and activity.[19,22] Other mechanisms include reduction of pro-inflammatory mediators (TNF-a, inteferon, IL-1, IL-6),[19,25,26] inhibition of gram-positive and gram-negative bacterial growth,[27-29] viral replication[22] and pro-inflammatory cytokines.[30]

Astragalus membranaceous (astragalus)

The root of *A. membranaceous* is an important therapeutic herb in the traditional Chinese medicine system for many health issues including immune support, the treatment of viral infections, debility and wound healing.[31,32]

The primary active constituents are considered to be the triterpene saponins (astrogalosides), flavonoids and polysaccharides,[11,31,33] and clinical data supports the traditional use of the herb for modulation of the immune system due to the effects of these constituents.[11,31,32]

The specific mechanisms contributing to the therapeutic effects of *A. membranaceous* include increasing monocyte, neutrophil and lymphocyte levels, stimulating macrophage maturation and T-cell activity[11,31,35,36] and antibody production[11,34] as well as modulating the synthesis of inflammatory mediators (NO, IL-2, IL-4, IL-10, IL-12, NF-kB).[31,34,37-39]

Inula helenium (elecampane)

Inula helenium root has a long history of use in Mongolian traditional medicine for immune related conditions, as well as in the west for respiratory health.[40,41]

The biologically active constituents that have been isolated include coumarins, flavonoids, polysaccharides, fatty acids and saponins.[40]

The polysaccharides have been observed to induce a Th1 immune response, macrophage production of NO[42] and stimulation of the complement system activity.[40]

Other mechanisms of action include inhibition of *S. aureus* infection[43] and anti-inflammatory activity through p38 MAPK-dependent HO-1 signalling pathway induction.[44]

Olea europaea (olive leaf)

Olive leaf has been used in traditional and folk medicine for fevers and diseases such as malaria.[45,46]

The main active constituents of *O. europaea,* the secoiridoids like oleuropein, as well as flavonoids and phenolic compounds,[45,46] contribute to the immune associated antimicrobial, antibacterial, antiviral and anti-inflammatory effects of the herb.[45]

The mechanisms of these constituents observed in preliminary data include stimulation of macrophage activation, inhibition of a wide range of bacterial and microbial pathogens (*E. coli*, *S. aureus*, *Salmonella* and *B. subtilis, C. jejuni*)[45,47,48] and preventing viral host cell entry.[45] Anti-inflammatory mechanisms include inhibition of the classical complement system pathway and pro-inflammatory cytokine synthesis (NO, IL-17)[45,49]

Sambucus nigra (elder)

Both the fruit and flowers from *Sambucus nigra* have been documented in traditional western medicine for use against the cold and as a diaphoretic in catarrhal complaints.[50]

Several types of anthocyanins have been identified as the primary active constituents of *S. nigra*, with smaller quantities of carbohydrates, vitamins and minerals.[50]

Clinical trials have observed improvements in cold and flu symptom severity and duration with use of the herb.[50,51]

The specific effects of *S. nigra* on the immune system includes inhibiting H1N1 viral replication, propagation and host cell entry,[50,52,53] stimulation of macrophage activity, increased production of pro-inflammatory cytokines (TNF-a, IL-1, IL-6, IL-8, IFN-gamma)[50,54] and antimicrobial activity against gram-positive and gram-negative bacteria.[52]

Thymus vulgaris (thyme)

Different types of preparations of *T. vulgaris* have been used in traditional medicine for conditions such as laryngitis, bronchitis, pertussis, tonsillitis and coughs related to colds.[9,11]

The German Commission E Monographs approves the use of *T. vulgaris* for the symptoms of bronchitis, whooping cough and upper respiratory catarrh.[9]

The phenols thymol and carvacrol, flavonoids, caffeic acid, rosmarinic acid, polysaccharides and triterpenes are the main constituents of the herb.[11,55]

Animal and *in vitro* data has demonstrated that the mechanism of *T. vulgaris* and its constituents involves inhibition of PPAR-gamma-dependent COX-2 expression, NF-kB transcription and subsequent cytokine gene expression and secretion,[55-57] and inhibition of gram-positive and gram-negative bacteria growth and colonisation (*C. albicans, S. aureus, E. coli, Enterococcus*).[55,58]

The physiological effects of *Echinacea purpurea, Andrographis paniculata, Astragalus membranaceous, Inula helenium, Olea europaea, Sambucus nigra* and *Thymus vulgaris* on innate and adaptive immunity are diverse. The variability of these mechanisms highlights the importance of utilising a combination of herbs therapeutically to support the complex immune system for clinically relevant outcomes.

References available on request.

NAC for persistent infections

The important antioxidant N-acetylcysteine is at the centre of an expanding field of research investigating its benefits in chronic and persistent infections.

Belinda Reynolds, BScNut&Diet(Hons)

N-acetylcysteine (NAC) is well recognised as an antioxidant, and precursor to glutathione. As such it is often prescribed for addressing conditions associated with toxic overwhelm (e.g. paracetamol overdose), oxidative stress and immune dysfunction.

Based on its role as a precursor to the antioxidant glutathione, and its action as a modulating agent of glutamatergic, dopaminergic, neurotropic and inflammatory pathways, NAC has shown promising benefits in psychiatric disorders including addiction/substance abuse,[1] autism, obsessive-compulsive spectrum disorders, schizophrenia, depression and bipolar disorder.[2]

NAC has been demonstrated to assist in the improvement of fertility in patients with polycystic ovarian syndrome (PCOS) at 1200-1800mg daily in divided doses,[3,4] and is useful also in chronic obstructive pulmonary disorder (COPD) at doses of 600mg twice daily.[5]

NAC's mechanisms of action in the management of COPD include its antioxidant and inflammatory actions to assist in minimising local airway swelling, together with its mucolytic benefits. NAC is able to break the disulphide bond in the mucin monomer, ultimately reducing mucous viscosity. Furthermore the antioxidant has a mucoregulatory effect, inhibiting hyperplasia of mucous-secreting cells,[6,7] and reducing the expression of the MUC5AC gene (involved in mucous secretion).[7] In addition, glutathione is essential to the functioning of specific immune cells, and via its role in supporting healthy glutathione synthesis, NAC can assist in minimising infection risk. It is NAC's mucolytic role, in combination with additional influences on oxidative stress that appear to make it useful in persistent, antibiotic-resistant infections.

Research demonstrates that NAC can be used in combination with antibiotics or other antimicrobial agents to enhance a pathogenic bacterial colonies' susceptibility to the effects of such treatments.

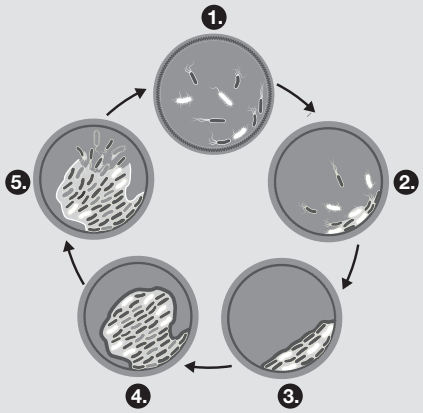
What makes an infection persist?

One key way in which an infection becomes persistent (e.g. drug resistant *Helicobactor pylori*, chronic upper respiratory and gastrointestinal infections) is via the formation of biofilms. These biofilms can protect microbial colonies from exposure to the environment (including the immune system) and antimicrobial agents (e.g. antibiotics, antimicrobial herbs), while assisting the colony in attachment to a surface. In fact, depending on the organism and type of antimicrobial and experimental system, biofilm bacteria can be up to a thousand times more resistant to antimicrobial stress than free-swimming bacteria of the same species.[8]

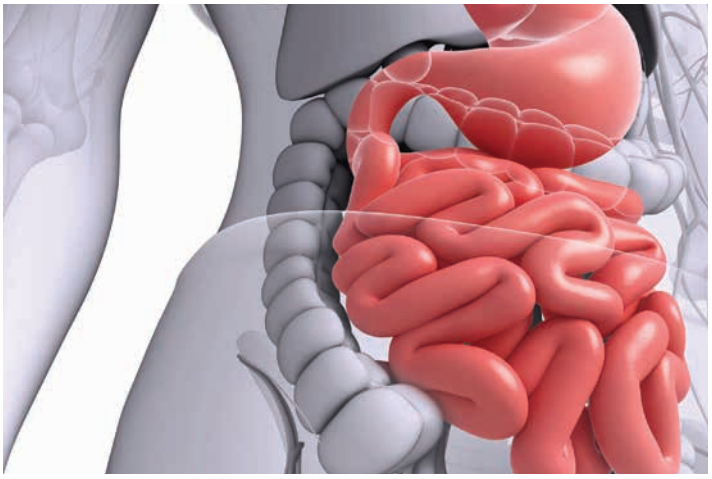
It is estimated that 60% of all human infections and 80% of refractory/chronic infections (i.e. unresponsive to medical treatment) are attributable to biofilm colonies.[9] When it comes to chronic infections, it has become clear through research that bacteria are able to persist on mucosal surfaces through formation of these biofilms; interestingly, biofilms are considered to be the most ubiquitous and successful forms of life on earth.[10] The biofilm is an extracellular polymeric substance (EPS) matrix which is composed of a wide variety of materials including polysaccharides, proteins, nucleic acids and lipids.[10] The general process of biofilm formation involves adhesion of free-living or "planktonic" bacteria to a surface, which subsequently develop into microcolonies and form a biofilm. As the biofilm continues to grow several things can happen; the biofilm may spread into uninfected areas as environmental conditions allow and, occasionally, cells will detach from the biofilm and re-enter a planktonic (i.e. "free swimming") mode. These planktonic cells can then repeat the cycle, infecting new surfaces (figure 1).[11]

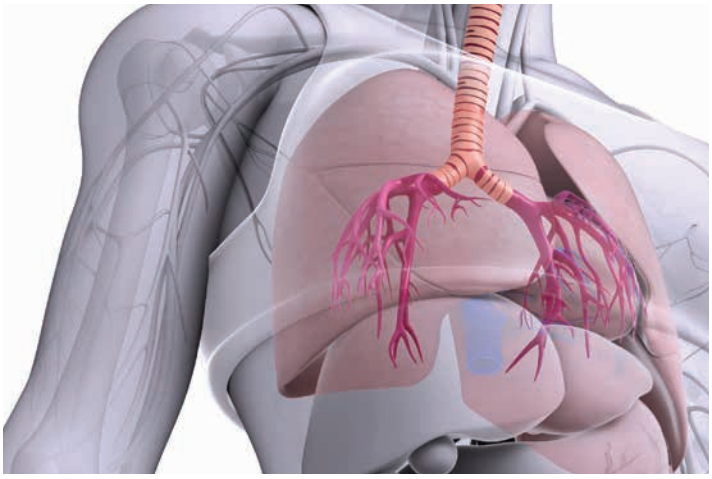
There are multiple natural substances which have been identified as useful for the inhibition and/or disruption of biofilms, and these include berberine[12] (e.g. from golden seal and phellodendron), ellagic acid (e.g. from pomegranate)[13] as well as proteolytic enzymes such as serrapeptase.[14]

FIGURE 1. BIOFILM FORMATION AND DISPERSION CYCLE



1. Single free floating bacteria land on surface
2. Bacteria cells aggregate and attach
3. Growth and division of bacteria for biofilm formation
4. Mature biofilm formation
5. Part of biofilm disperses to release free floating bacteria for further colonisation





Furthermore, NAC is noted to be not only a mucolytic agent (useful for breaking down the slimy components of the biofilm), but also to possess the ability to reduce the production of the EPS, and to promote the disruption of mature biofilms.[15]

Targeting bacterial communication

An important step involved in the bacterial formation of microcolonies, their virulence and biofilm formation, is the release of quorum sensing chemicals. Put simply, quorum sensing is a process through which bacteria communicate in order to determine the local population density. Once quorum sensing substances reach a certain concentration (due to high populations of like microbes), this is detected by the inhabitants and can result in activation of gene transcription within the micro-organisms. This gene expression sees the "switching on" of virulence factors (e.g. the release of harmful toxins), or can begin the process of microcolony and subsequent biofilm formation.[16] Due to the growing concern of antibiotic resistance, researchers are also looking to understand not only what substances may be used to inhibit and disrupt biofilms, but also what may possess the ability to inhibit quorum sensing.

NAC has demonstrated in early studies, the ability to inhibit quorum sensing chemicals to thus prevent infection development (e.g. *Pseudomonas aeruginosa* commonly infecting cystic fibrosis sufferers). It is suggested that this function is owed to the antioxidant capabilities of NAC. Reactive oxygen species seem to be responsible for activating the quorum sensing pathways, which is inhibited by NAC's ability to suppress hydrogen peroxide activity and the master quorum sensing regulators. This effect on hydrogen peroxide was also able to inhibit the toxin release from *P. aeruginosa*, as virulence factors, such as toxin secretion, are also stimulated by oxidative stress.[17]

NAC and treatment-resistant *H. pylori*

Standard triple therapy consisting of proton pump inhibitors (PPIs), amoxicillin, and clarithromycin, has long been recommended as first-line therapy for *H.pylori* infection. However, the eradication rate of this triple therapy has been decreasing because of increasing antibiotic resistance.[18] In two randomised controlled trials on *H. pylori*, pretreatment with NAC, before an antibiotic therapy against the *H. pylori*- mediated biofilms, showed that NAC achieved an increase in permeability of antibiotic treatment, resulting in the overcoming of drug resistance and eradication of pre-formed biofilms. In addition there was an observed reduction in gastric barrier mucus thickness and reduction of mucus viscoelasticity.

Chronic upper respiratory tract infections

It is no surprise that biofilms play an important role in chronic otitis media (ear infections), sinusitis, tonsillitis and adenoiditis (infected adenoids). Studies have been carried out on both the use and the efficacy of NAC in the breakdown of biofilms related to pathogenic culprits of these persistent conditions, and it has been shown that NAC, used at different concentrations, is able to reduce bacterial adhesion in several of these areas, making NAC an important consideration in chronic cases.[19]

P. aeruginosa is a common pathogen in chronic respiratory tract infections (particularly in cystic fibrosis (CF) sufferers). It typically makes a biofilm, making infection treatment difficult. In a study investigating the inhibitory effects of NAC on biofilms produced by *P. aeruginosa*, results demonstrated that NAC holds antibacterial properties against the pathogen, and may detach *P. aeruginosa* biofilms. It is therefore suggested that NAC may be a new strategy for the treatment of biofilm-associated chronic respiratory infections due to *P. aeruginosa*, and further research is warranted.[20]

Dental caries

Dental plaque is one of the more obvious and tough-to-treat forms of biofilm. As a compound with a wide safety margin, NAC has demonstrated the potential as a therapy to be used as an antiplaque, bacteriostatic agent for managing chronic dental decay. The potential anticaries benefit of NAC is directly related to reducing the biofilm coverage which reduces the degree of acid generation and the amount of time that the surface is exposed to the lower pH.[21]

In conclusion, NAC represents an interesting consideration to promote the resolution of persistent infections which may have previously resisted standard antimicrobial treatments. It not only demonstrates the ability to interfere with bacterial communication and suppression of virulence factors, but inhibits biofilm formation, disrupts mature biofilms, assists with mucus breakdown and provides local anti-inflammatory and antioxidant benefits.

References available on request.

Earn with our ordering system

You prescribe, the patient orders, we deliver and you get the rebates paid directly into your account – that's how easy and convenient BioCeuticals Patient Billing is.

How can we help you build your role as a primary healthcare provider in your community? BioCeuticals is committed to supplying evidence-based, high quality and practitioner-only complementary medicines, and we believe that by supporting your business, we are also helping to raise the standards of complementary therapies for the benefit of qualified practitioners as well as the entire profession.

BioCeuticals Patient Billing is one of Australia's most advanced online ordering tools. Not only is it convenient and simple to use, but it allows small business owners such as qualified practitioners to have a steady income stream each month, with no additional hassles or cost to your business.

What is Patient Billing?

BioCeuticals Patient Billing offers practitioners the ease and flexibility to prescribe the widest range of BioCeuticals products to their patients without the fuss of dispensary and stock management, shipping and handling.

When you set up your Patient Billing account, you control the markup and access that your patient has all on an easy-to-use interface co-branded with your company logo.

Your patients will enjoy the ability to access their prescriptions from the privacy of their own home and have this shipped direct to their door.

- Completely eliminate admin time dedicated to dispensary and stock management
- Flexibility and control to set your own markups and choose what product each patient can access
- Co-branded patient interface with your own company branding
- Receive your generated income each month to your nominated account, with a quick and easy delivery direct to your patients' door!

Set your Referral Codes

Your patient will need a "Referral Code" from you to identify you as their practitioner. You can set multiple Referral Codes with different markups. For example, you may want to reward your regular patients by offering a lower markup compared to new patients.

Therefore, you may create a Referral Code specifically for regular patients.

Setting individual markups for your patients Patient Billing allows you to set up a markup percentage value of your choice for your patient to use when ordering their prescribed product. This referral code can range from 0% markup to 100%. The markup determines the prices your patients pay. At the end of each month, you will receive a rebate amount direct to your bank account.

How to activate Patient Billing

Step 1.
Login to the BioCeuticals website at www.bioceuticals.com.au and go to "My Account". Click on "My Patients", under Patient Billing.

Activate your Patient Billing Settings and click "Update Settings".

Step 2.
Click on the link under "What do I do now?" to view or set up your Referral Codes.

Step 3.
Once you are on the Patient Billing setup page, click on "Create New Code", apply a name to your code and alter the markup percentage for a particular patient or category of clients.

Step 4.
Choose your preferred option of dispensing prescriptions online.

Step 5.
Click "Generate Code". A direct link to your shopping cart will be generated. Links to your shopping cart are provided in three formats:

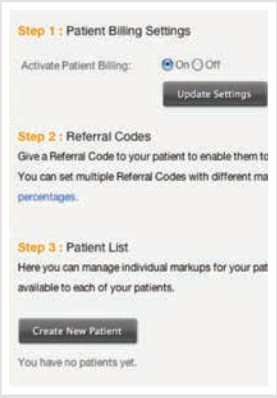
- URL for email
- HTML link to include in your website
- Quick Response (QR) Code to print on any marketing material

Please copy and share one of these links with your patient, in the most suitable format.

An email will be automatically delivered to you confirming your patient's registration and any subsequent orders.

Step 6.
Click the "Back" button on your browser to return to your Patient Billing settings. Click on "Create New Patient". Here you can manage your Patient List, and manually select which of our brands is available to each of your patients.

Register on www.bioceuticals.com.au today and gain easy access to your online shopping cart and your own online dispensing system.

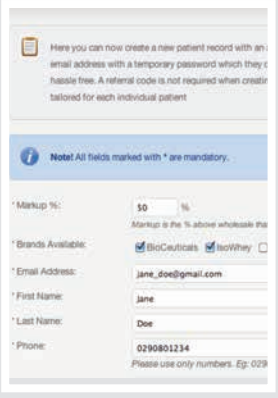


Step 1.

Step 2 & 3.

Step 4.

Step 5.



Step 6.

Should you be choosing activated nutrients?

Esther Parker

Nobody likes a time waster! In our busy day-to-day lives, we appreciate efficiency, so we can spend more time doing what we love. Taking remedies for our health should benefit us, not burden us! It's time to think in terms of a 'less is more' approach[1] – by using specific and beneficial nutrients which support your general health. Sound good? Welcome to the world of 'activated nutrients'. In particular, activated B vitamins.

Active forms of B vitamins bypass many or all of the metabolic pathways required for these nutrients to be effectively used by the body.[2] This may be of benefit to those who have a genetic variation which impairs their ability to convert a specific ordinary B vitamin into the form utilised by the body in metabolism.[3] Although the body still needs to metabolise, break down and re-make activated B vitamins to absorb and use them.[4]

The activated forms of B vitamins include the following; riboflavin sodium phosphate (B2), pyridoxal-5-phosphate (B6), folinic acid (B9) and mecobalamin (B12).[5-8] Several conversion steps have already taken place, so you rely less on your body (and other nutrients) to do all the work.

B vitamins are essential for our health. We need them to produce healthy DNA, metabolise food to make energy, support a healthy nervous system and the list goes on.[5-10] They are essential nutrients for us; from our earliest beginnings in the womb, right through into old age.[1,7] B vitamins also work best in unison[11]; this is why B vitamins are usually found together in the same supplement, for example, in a 'B complex'. Not only do B vitamins need each other to help break down, but to get into their active forms, they need other key vitamins and minerals as well.[11] You can see that this is a lot of work for our bodies to do!

Another reason we need B vitamins is for a function called 'methylation'. This process makes methyl groups, which are important biochemical molecules[11] used in just about all healthy body systems and functions; in the immune system, for the stress response, in healthy DNA production, to repair cell damage from free radicals, and more. Methylation needs B vitamins, particularly folate (B9), B6 and B12.[8,9]

Unfortunately, we all experience times of being unwell, or times when our food intake is less than perfect. For some, such as the elderly, or those with digestive issues, supplementation with activated B vitamins may be desirable.

For example, the absorption of vitamin B2 occurs in the upper gastrointestinal tract, and a compromised digestive system can adversely affect the body's ability to convert vitamin B2 to its active form, riboflavin sodium phosphate.[12]

If your diet is less than ideal and you are looking for nutritional support, then it might be worth a look into activated B vitamins. They might just be the boost you are looking for, but seek your healthcare practitioner's advice first as activated B vitamins may not be for everyone.

Vitamin supplements should not replace a balanced diet. If symptoms persist, please consult your healthcare practitioner.

Women's essentials

EVERYDAY NUTRITIONAL SUPPORT WITH ACTIVATED B VITAMINS
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- Formulated with key women's health concerns in mind, to provide nutritional support for healthy: red blood cell formation, thyroid function, glucose metabolism in healthy individuals and bones.
- Now contains activated vitamins B2, B6, B9 and B12.
- Upgraded formula provides 1000IU of vitamin D3, and vitamin K in the form of K2 for greater bioavailability.
- Provides vitamins A, C and D3, to support a healthy immune system plus zinc and selenium to healp maintain healthy antioxidant activity.

Men's Essentials

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- Provides nutritional support for healthy: male physiology, cognition, cellular energy production, prostate, testosterone production and sperm development and movement.
- Contains activated B vitamins – vitamin B2 (riboflavin sodium phosphate), vitamin B6 (P5P), vitamin B9 (folinic acid/ 5-MTHF), vitamin B12 (mecobalamin).
- Folinic acid, 5-MTHF, P5P and mecobalamin assist energy production.
- Vitamin K2 and D3 support normal healthy bones.

Can selected probiotics prevent eczema in early childhood?

Petra Hunter, ND BHSc (Nat)

Eczema is a multifactorial inflammatory skin disorder arising from the interplay of genetic predisposition and environmental factors. It frequently affects infants in the first few months of life and is strongly associated with later development of other allergic disorders, particularly asthma and allergic rhinitis.[1]

Eczema currently affects about 20% of Australian children under two years of age,[2] and it is expected that up to 80% of children suffering with eczema will develop other allergic disease.[3]

While the hygiene hypothesis – where an imbalance between the allergy promoting T-helper 2 (Th2) and non-allergy promoting T-helper 1 (Th1) driven immune responses result from a lack of childhood exposure to infections and microbial components due to increased hygiene practices – is a popular theory behind the steadily increasing rate of allergic disease in western society, not all epidemiological studies fully support this supposition. Expanded knowledge about the interaction between the intestinal microbiota and the immune system through the interaction of T-regulatory cells, bacterial metabolites and cytokines may bridge the gaps.[4]

The diversity of the gut flora has been found to be significantly reduced in infants with eczema and it has been shown that commensal bacteria belonging to *Bifidobacterium* and *Lactobacillus spp.* are present at a significantly greater abundance in non-eczematous infants and children up to five years of age.[5]

Pathogenic bacteria, on the other hand, such as *Enterococcus* and *Shigella spp.* have been found to be more abundant in eczematous infants.[5] Swedish researchers have also reported a higher prevalence of *S. aureus* and *C. difficile* in children who develop allergic disease.[6]

A number of studies have demonstrated an overall benefit of probiotic supplementation for the prevention of eczema in high risk infants. One such study, a clinical trial performed by the Wilhelmina Children's Hospital in conjunction with the Wageningen University in the Netherlands, examined the effects of a carefully selected three-strain probiotic combination in 102 women and their offspring who were at high risk of allergic disease.[6] The frequency of eczema, food allergies, allergic rhinitis or asthma were the primary endpoint during two years of follow-up. The probiotic combination consisted of *B. bifidum* W23, *B. lactis* W52 (previously classified as *B. infantis*), and *Lactococcus lactis* W58. These three very specific strains were selected on the basis of their capacity to stimulate Th1 and T regulatory cells, inhibit production of Th2 cytokines, and improve gut barrier function.[6]

The formula was administered to the mother during the last six weeks of pregnancy and to the infant for 12 months. Eczema incidence was reported by the parents in a weekly diary during the first three months of life and was significantly lower in the intervention group compared with placebo; 6/50 (12%) vs 15/52 (29%) ($P = 0.035$). The incidence of eczema at one and two years was 23/50 (intervention group) vs 31/48 (placebo group) and 27 (intervention) vs 34 (placebo) respectively. Thus, at the age of three months, relative risk reduction was 58%, which decreased to 26% and 22% at one and two years respectively. No differences were observed in respiratory symptoms indicative of asthma or allergic rhinitis at the age of two years.

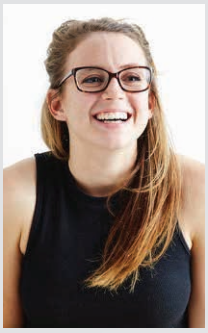
The study participants were re-evaluated yet again at the age of six. However, this follow-up study showed no statistically significant differences in prevalence of eczema, asthma, allergic rhinitis, and food allergy between the intervention group and the placebo group.[7]

The researchers concluded that one year administration of this selected probiotic combination did demonstrate a beneficial effect on the development of eczema up to the age of two years. Yet, the beneficial effect did not extend to the age of six years and does not lead to primary prevention of asthma.

Based on these results, the research suggests that as the development of the gut microbiota composition may continue for at least the first three years of life, prolonged probiotic therapy may be required to achieve long-lasting impact.[7]

References available on request.

Practical Q&A



BioCeuticals Practitioner Educator Emily Seddon is a qualified naturopath with a love of science. Growing up with a hippy mum and dad, she became used to thinking outside the box for her own health. She has since completed a degree in Health Science, majoring in naturopathy; combining that passion for healthy living with scientific and traditional evidence to help others to live happy and healthy lives. She lives by the philosophy of 'there is no such thing as too much tea' and is currently trying to teach herself to surf and play golf (so far unsuccessfully).

Emily Seddon, BHSc Nat

Q. ARE THERE ANY WARNINGS WHEN USING IMMUNE BOOSTER ARMAFORCE?

Yes, the use of **ArmaForce** is contraindicated in pregnancy due to its *Andrographis paniculata* (andrographis) content. Due to lack of evidence regarding its safety in lactation, andrographis is also best avoided in these circumstances.[1]

Both andrographis and *Echinacea purpurea* (echinacea), although well tolerated in most people, have a potential risk of allergic reactions, including skin rash and anaphylaxis in rare cases.[1] High dosing of ArmaForce should be avoided, with a maximum of 4 tablets taken daily. Other warnings include:

- Caution is recommended when using ArmaForce alongside hypotensive and hypoglycaemic medications, andrographis and olive leaf may have a possible additive effect with these medications.[1]
- Concurrent use of andrographis with anticoagulant or antiplatelet medications may increase risk of bruising and bleeding due to andrographolides inhibiting platelet-activating-factor-induced platelet aggregation.[1]
- A theoretical interaction may occur between the immunostimulant activity of andrographis, echinacea and immunosupressive medications.[1]

Additionally, ArmaForce is not to be used in children under two years of age without medical advice. If coughing or symptoms persists the patient should consult their doctor or healthcare practitioner.

Q. WHAT ALTERNATIVE CAN BE USED FOR CHILDREN AND ADULTS IN PLACE OF ARMAFORCE?

ImmunoFactors for Juniors contains *Sambuccus nigra* elder flower and fruit, which has been traditionally used in western herbal medicine to help relieve the symptoms of the common cold, including sinus congestion, and to support the immune system.[2,3] It also contains vitamins A and C, and zinc as nutritional support for a healthy immune system, and has adult and children's dosage recommendations on the bottle.

Maintaining healthy levels of vitamin D3 may help to prevent the occurrence of respiratory tract infections, such as the common cold, in both children and adults.[4,5]

Liquid vitamin D3 solutions may solidify when kept in cool conditions (eg. a fridge), so allow the product to cool to room temperature for easy dispensing of drops.

These ingredients have not been shown to be contraindicated during pregnancy or lactation.

Q. WHY ARE PROBIOTICS SO IMPORTANT FOR IMMUNITY?

Probiotics are vital for immune function for many reasons. Not only do they contribute to a healthy, balanced microbiome, they also communicate with the gastrointestinal epithelium and gut-associated lymphoid tissue (GALT) to activate and modulate innate and adaptive immune responses.[6]

Q. WHAT CAN BE USED FOR COLD SORES?

ViroGuard is a unique combination of micronutrients and herbs that provide support for healthy immune function. ViroGuard has been formulated to help relieve the frequency, duration and severity of cold sores.[7]

ViroGuard can be prescribed up to 3 capsules internally daily and/or applied topically to a cold sore at intervals throughout the day.

References available on request.

How Aussie praccies are helping Syrian refugees

Director of Involvement Volunteers International, nutritionist Lauren Lacey, gathered 30 practitioners and donations and flew to the frontline of Greece's refugee camps. And she's ready to do it again!

Syria's civil war has created the worst humanitarian crisis of our time. More than 11 million people — half the country's pre-war population — have been killed or forced to flee their homes. Almost five million of these are now refugees; half of those affected are children.

The facts are staggering and the crisis "should be garnering a groundswell of support around the world" according to Filippo Grandi, the United Nations High Commissioner for Refugees (UNHCR).

Back home in Australia, a group of practitioners from the complementary, integrative and medical industries decided to support the cause in the best way they know how. Led by nutritionist and director of Involvement Volunteers International Lauren Lacey, 30 practitioners flew to Greece to volunteer across six major refugee camps.

Armed with donations of BioCeuticals supplements – including vitamin D and magnesium – Isowhey protein powders, whole food powders, food preparation equipment, clothing, seeds, nappies, fresh food and more, the volunteers spent three weeks in Souda Camp, Ritsona, Larissa, Veira, Softex, Oinofyta and Serbian Barracks. They split into teams of 4-5 across the islands and worked 10am-4pm with very little breaks.

"Each camp had about 1200 refugees. We set up an infant nutrition and mother's centre in one camp, where we treated between 100-200 refugees, children under 6 and their mums, every day," said Lauren.

"Malnutrition amongst lactating mothers and their children is a high concern in the camps, and one of our main duties was to identify high risk refugees and improve refugee care."

A high rate of protein deficiencies was noted as well as stunted growth. The volunteer team of general practitioners, naturopaths and nutritionists made daily blends of yoghurt mixed with IsoWhey protein powders for morning tea, which was a popular change for the refugees.

At the children's centre camp, for kids over 6 years and their parents, the team treated up to 300 refugees a day. Here they replaced sugar-loaded muesli bars with nutritious protein balls.

"We literally made thousands of protein balls every day, using IsoWhey Wholefoods superfood powders and protein powder. We had two food processors and they were used non-stop. Each child received one protein ball in their pack every day. In the afternoon, we gave out tea and IsoWhey Meal Replacement Bars cut up and distributed around the camp for men, women and children," said Lauren.

"Some of the most common conditions, besides nutrient deficiency, were untreated and infected wounds, mental health conditions, respiratory illness/immune deficiency amongst the children, and hypothermia in winter; some mothers and children were moved to hostels during the coldest nights."

While the group returned at the end of February, there is more work to be done. Lauren is organising for another group to return in June/July and is seeking both volunteers and donations.

Interested practitioners should email Lauren@volunteering.org.au

"Each camp had about 1200 refugees. We set up an infant nutrition and mother's centre in one camp, where we treated between 100-200 refugees, children under 6 and their mums, every day,"

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w: http://breathingwell.net.au/courses

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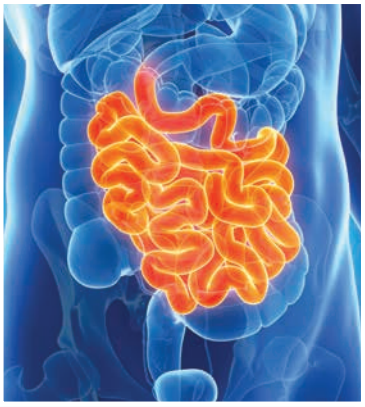
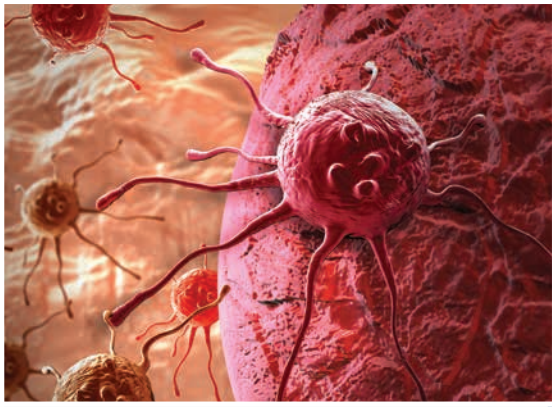

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