

Ingredient spotlight:

- Bone, K & Mills, S, Principles and Practice of Phytotherapy, 2nd Ed., 2013, Churchill Livingstone Elsevier
- Chandrasekhar K, et al, A prospective randomised double-blind, placebo-controlled study of safety and efficacy of high concentration full spectrum extract of ashwaganda root in reducing stress and anxiety in adults, Indian J Psychol. Med., 2012, Vol.34, pp.255-262
- Kelani et al, ashwaganda root in the treatment of non-classical adrenal hyperplasia, 2012, BMJ Case Rep., 17. Pii: bcr2012006898
- Malik F, et al, A standardised root extract of Withania somnifera and its major constituent withanolide-Aelicit humoral and cell-mediated immune responses by up regulation of Th1 dominant polarisation in BALB, 2007, Life Sci., Vol.80(16), pp.1525-1538
- Mirjalili, M et al, Steroidal lactones from Withania somnifera, an ancient plant for novel medicine, 2009, Molecules, Vol.14(7), pp.2373-2393
- Panda S, et al, Changes to thyroid hormone concentrations after administration of ashwaganda root extract to adult male mice, 1998, J. Pharm. Pharmacol., Vol.50(9), pp.1065-1068
- Rasool, M, Suppressive effect of Withania somnifera root powder on experimental gouty arthritis: an in vivo and in vitro study, 2006, Chem. Biol. Interact., Vol.164(3), pp.174-180
- Singh D et al, Withania somnifera inhibits NF-kappaB and AP-1 transcription factors in human peripheral blood and synovial fluid mononuclear cells, 2007, Phytother. Res., Vol.21(10), pp.905-913
- Staner, L, Sleep and anxiety disorders, 2003, Dialogues in Clinical Neuroscience, Vol.5(3), pp.249-258

Sleep feature:

1. Choices N. Snoring - NHS Choices [Internet]. Department of Health; (no date) [cited 2016 Oct 11]. Available from: <http://www.nhs.uk/conditions/snoring/Pages/Introduction.aspx>
2. Sleep Apnoea Trust Downloadable Leaflets, Forms and Newsletter - Sleep Apnoea Trust [Internet]. Available from: <http://www.sleep-apnoea-trust.org/sleep-apnoea-trust-downloadable-leaflets-forms-newsletter/>
3. Choices N. Insomnia - Causes - NHS Choices [Internet]. Department of Health; (no date) [cited 2016 Sep 30]. Available from: <http://www.nhs.uk/Conditions/Insomnia/Pages/Introduction.aspx>
4. Choices N. Restless legs syndrome - NHS Choices [Internet]. Department of Health; (no date) [cited 2016 Oct 11]. Available from: <http://www.nhs.uk/conditions/Restless-leg-syndrome/Pages/Introduction.aspx>
5. The Great British Bedtime Report [Internet]. Skipton, UK; 2013 [cited 2016 Oct 11]. Available from: <http://www.sleepcouncil.org.uk/wp-content/uploads/2013/02/The-Great-British-Bedtime-Report.pdf>
6. Hoevenaar-Blom MP, Spijkerman AMW, Kromhout D, Verschuren WMM. Sufficient sleep duration contributes to lower cardiovascular disease risk in addition to four traditional lifestyle factors: the MORGEN

- study. *Eur J Prev Cardiol*. 2014 Nov;21(11):1367–75.
7. Straif K, Baan R, Grosse Y, Secretan B, El Ghissassi F, Bouvard V, et al. Carcinogenicity of shift-work, painting, and fire-fighting. *Lancet Oncol*. 2007 Dec;8(12):1065–6.
8. Möller-Levet CS, Archer SN, Bucca G, Laing EE, Slak A, Kabiljo R, et al. Effects of insufficient sleep on circadian rhythmicity and expression amplitude of the human blood transcriptome. *Proc Natl Acad Sci U S A* [Internet]. 2013 Mar 19 [cited 2016 Oct 11];110(12):E1132-41. Available from: <http://www.pubmedcentral.nih.gov/articlerender.fcgi?artid=PMC3607048>
9. Grandner MA, Jackson N, Gerstner JR, Knutson KL. Dietary nutrients associated with short and long sleep duration. Data from a nationally representative sample. *Appetite*. 2013;64:71–80.
10. Burke TM, Markwald RR, McHill AW, Chinoy ED, Snider JA, Bessman SC, et al. Effects of caffeine on the human circadian clock in vivo and in vitro. *Sci Transl Med*. 2015;7(305).
11. McNamara JPH, Wang J, Holiday DB, Warren JY, Paradoa M, Balkhi AM, et al. Sleep disturbances associated with cigarette smoking. *Psychol Health Med*. 2014 Jul 4;19(4):410–9.
12. Ebrahim IO, Shapiro CM, Williams AJ, Fenwick PB. Alcohol and Sleep I: Effects on Normal Sleep. *Alcohol Clin Exp Res*. 2013 Apr;37(4):539–549.
13. Hargens TA, Kaleth AS, Edwards ES, Butner KL. Association between sleep disorders, obesity, and exercise: a review. *Nat Sci Sleep* [Internet]. 2013 [cited 2016 Sep 30];5:27–35. Available from: <http://www.pubmedcentral.nih.gov/articlerender.fcgi?artid=PMC3630986>
14. Abbasi B, Kimiagar M, Sadeghniiat K, Shirazi MM, Hedayati M, Rashidkhani B. The effect of magnesium supplementation on primary insomnia in elderly: A double-blind placebo-controlled clinical trial. *J Res Med Sci* [Internet]. 2012 Dec [cited 2016 Oct 11];17(12):1161–9. Available from: <http://www.pubmedcentral.nih.gov/articlerender.fcgi?artid=PMC3703169>
15. Tatsuki F, Sunagawa GA, Shi S, Susaki EA, Yukinaga H, Perrin D, et al. Involvement of Ca(2+)-Dependent Hyperpolarization in Sleep Duration in Mammals. *Neuron* [Internet]. 2016 Apr 6 [cited 2016 Oct 11];90(1):70–85. Available from: <http://www.ncbi.nlm.nih.gov/pubmed/26996081>
16. Jackson WF. Potassium Channels in Regulation of Vascular Smooth Muscle Contraction and Growth. In: *Advances in Pharmacology*. 2016.
17. Bent S, Padula A, Moore D, Patterson M, Mehling W. Valerian for sleep: a systematic review and meta-analysis. *Am J Med* [Internet]. 2006 Dec [cited 2016 Oct 1];119(12):1005–12. Available from: <http://www.pubmedcentral.nih.gov/articlerender.fcgi?artid=PMC4394901>
18. Kahn A, Mozin MJ, Rebuffat E, Sottiaux M, Muller MF. Milk intolerance in children with persistent sleeplessness: a prospective double-blind crossover evaluation. *Pediatrics*. 1989 Oct;84(4):595–603.

19. Hardeland R. Neurobiology, pathophysiology, and treatment of melatonin deficiency and dysfunction. *ScientificWorldJournal* [Internet]. 2012 [cited 2016 Oct 11];2012:640389. Available from: <http://www.ncbi.nlm.nih.gov/pubmed/22629173>
20. Järup L. Hazards of heavy metal contamination. *Br Med Bull* [Internet]. 2003 [cited 2016 Oct 11];68(1):167–82. Available from: <http://www.ncbi.nlm.nih.gov/pubmed/14757716>
21. Bidaki R, Zarei M, Khorram Toosi A, Hakim Shooshtari M. A review on genetics of sleep disorders. *Iran J psychiatry Behav Sci* [Internet]. 2012 [cited 2016 Oct 11];6(1):12–9. Available from: <http://www.ncbi.nlm.nih.gov/pubmed/24644464>
22. Dahle L O, Berg G, Hammar M, Hurtig M, Larsson L. The effect of oral magnesium substitution on pregnancy-induced leg cramps.
23. Jacka FN, Overland S, Stewart R, Tell GS, Bjelland I, Mykletun A. Association between magnesium intake and depression and anxiety in community-dwelling adults: the Hordaland Health Study. *Aust N Z J Psychiatry*. 2009 Jan;43(1):45–52.
24. Singewald N, Sinner C, Hetzenauer A, Sartori SB, Murck H. Magnesium-deficient diet alters depression- and anxiety-related behavior in mice—influence of desipramine and *Hypericum perforatum* extract. *Neuropharmacology*. 2004;47(8):1189–97.
25. Abbasi B, Kimiagar SM, Mohammad-Shirazi M, Sadeghniiat K, Rashidkhani B, Karimi N, et al. Effect of Magnesium Supplementation on Physical Activity of Overweight or Obese Insomniac Elderly Subjects: A Double-Blind Randomized Clinical Trial. *Zahedan J Res Med Sci*. 2013;15(3):14–9.
26. Bates B, Lennox A, Prentice A, Bates C, Page P, Nicholson S, et al. National Diet and Nutrition Survey: Results from Years 1-4 (combined) of the Rolling Programme. 2008 [cited 2016 Oct 11]; Available from: www.gov.uk/phe
27. McCarty DE, Reddy A, Keigley Q, Kim PY, Marino AA. Vitamin D, race, and excessive daytime sleepiness. *J Clin Sleep Med* [Internet]. 2012 Dec 15 [cited 2016 Oct 1];8(6):693–7. Available from: <http://www.pubmedcentral.nih.gov/articlerender.fcgi?artid=PMC3501666>

IBS feature:

Shona Wilkinson:

- (1) Tillisch K, Labus JS, Naliboff BD, et al. Characterization of the alternating bowel habit subtype in patients with irritable bowel syndrome. *Am J Gastroenterol* 2005;100:896–904.
- (2) Whorwell PJ, McCallum M, Creed F, et al. Non-colonic features of irritable bowel syndrome. *Gut* 1986;27:37–40.
- (3) Marshall JK, Thabane M, Garg AX, et al. Intestinal permeability in patients with irritable bowel syndrome after a waterborne outbreak of acute gastroenteritis in Walkerton, Ontario. *Aliment Pharmacol Ther* 2004;20:1317–22.
- (4) Francis CY, Whorwell PJ. Bran and irritable bowel syndrome: time for reappraisal. *Lancet* 1994;344:39–40.

(5) Browning S M. Constipation, diarrhoea and irritable bowel syndroms. *Prim Care* 1999;26:113-39.

Caroline Harmer:

1. Ibid.
2. Spiegel BM, Chey WD, Chang L. Bacterial overgrowth and irritable bowel syndrome: unifying hypothesis or a spurious consequence of proton pump inhibitors? *Am J Gastroenterol*. 2008 Dec;103(12):2972-6.
3. Tungtrongchitr, et al., "Blastocystis hominis infection in irritable bowel syndrome patients." *Southeast Asian J Trop Med Public Health*. 2004 Sep;35(3):705-10. There may also be an overgrowth of yeast particularly *Candida albicans*. H. Santlemann and J.M. Howard, "Yeast metabolic products, yeast antigens and yeasts as possible triggers for irritable bowel syndrome." *Eur J Gastroenterol Hepatol* 2005 Jan;17(1):21-6.
4. Elizabeth Lipski, *Digestive Wellness*, Keats Publishing, Inc., 1996, p.238
5. Ibid.
6. Micheal Murray, ND and Joseph Pizzorno, ND, *Encyclopedia of Natural Medicine*, Revised Second Edition, Prima Health, 1998, p. 611.
7. Op cit., Lipski, p239.

Claire Barnes:

- 1 Distrutti E, Monaldi L, Ricci P, Fiorucci S. Gut microbiota role in irritable bowel syndrome: New therapeutic strategies. *World J Gastroenterol* 2016; 22: 2219–41.
- 2 Longstreth GF, Thompson WG, Chey WD, Houghton LA, Mearin F, Spiller RC. Functional bowel disorders. *Gastroenterology* 2006; 130: 1480–91.
- 3 Hayes P, Corish C, O'Mahony E, Quigley EMM. A dietary survey of patients with irritable bowel syndrome. *J Hum Nutr Diet* 2014; 27 Suppl 2: 36–47.
- 4 Tazzyman S, Richards N, Trueman AR, *et al*. Vitamin D associates with improved quality of life in participants with irritable bowel syndrome: outcomes from a pilot trial. *BMJ open Gastroenterol* 2015; 2: e000052.
- 5 Marsh A, Eslick EM, Eslick GD. Does a diet low in FODMAPs reduce symptoms associated with functional gastrointestinal disorders? A comprehensive systematic review and meta-analysis. *Eur J Nutr* 2016; 55: 897–906.
- 6 Guglielmetti S, Mora D, Gschwender M, Popp K. Randomised clinical trial: *Bifidobacterium bifidum* MIMBb75 significantly alleviates irritable bowel syndrome and improves quality of life--a double-blind, placebo-controlled study. *Aliment Pharmacol Ther* 2011; 33: 1123–32.
- 7 Aragon G, Graham DB, Borum M, Doman DB. Probiotic therapy for irritable bowel syndrome. *Gastroenterol Hepatol (N Y)* 2010; 6: 39–44.
- 8 Kajander K, Krogius-Kurikka L, Rinttilä T, Karjalainen H, Palva A, Korpela R. Effects of multispecies probiotic supplementation on intestinal microbiota in irritable bowel syndrome. *Aliment Pharmacol*

- Ther* 2007; 26: 463–73.
- 9 Quigley EMM. Probiotics in Irritable Bowel Syndrome: The Science and the Evidence. *J Clin Gastroenterol*; 49 Suppl 1: S60–4.
 - 10 Yoon JS, Sohn W, Lee OY, *et al.* Effect of multispecies probiotics on irritable bowel syndrome: a randomized, double-blind, placebo-controlled trial. *J Gastroenterol Hepatol* 2014; 29: 52–9.

Anti-ageing feature:

Romina Melwani:

Sun J, Wang H, Ng TB. Isolation of a laccase with HIV-1 reverse transcriptase inhibitory activity from fresh fruiting bodies of the *Lentinus edodes* (Shiitake mushroom). *Indian J Biochem Biophys.* 2011 Apr;48(2):88-94.

El-Mekkawy, S., Mesellhy, M.R., Nakamura, N., Tesuka, Y., Hattori, M., Kakiuchi, N., Shimotohno, K., Kawahata, T., and Otake, T., Anti-HIV and anti-HIV-protease substances from *Ganoderma lucidum*, *Phytochemistry*, 49, 1651–1657, 1998.

Jenny Bodenham:

- (1) Josine E. Verhoeven, *et al.* Anxiety disorders and accelerated cellular ageing. *The British Journal of Psychiatry* May 2015, 206 (5) 371-378; DOI: 10.1192/bjp.bp.114.151027
- (2) Solfrizzi V, *et al.* The role of diet in cognitive decline. *Journal of Neural Transmission.* 2003 Jan;110(1):95-110.
- (3) Skoog I, Lernfelt B, Landahl S, Palmertz B, Andreasson LA, Nilsson L, Persson G, Oden A, Svanborg A (1996) 15-Year longitudinal study of blood pressure and dementia. *Lancet* 347: 1141–1145
- (4) Ott A, Stolk RP, van Harskamp F, Pols HA, Hofman A, Breteler MM (1999) Diabetes mellitus and the risk of dementia: the Rotterdam Study. *Neurology* 53: 1937–1942
- (5) Ott A, Breteler MM, de Bruyne MC, van Harskamp F, Grobbee DE, Hofman A (1997) Atrial fibrillation and dementia in a population-based study. *The Rotterdam Study. Stroke* 28: 316–321
- (6) Crous-Bou, T. T. Fung, *et al.* Mediterranean diet and telomere length in Nurses' Health Study: population based cohort study. *BMJ*, 2014; 349 (dec02 5): g6674 DOI: 10.1136/bmj.g6674
- (7) Vina J, Borras C, Miquel J. Theories of ageing. *IUBMB Life.* 2007;59(4–5):249–254.
- (8) Ribero S. *et al.*, Acne and telomere length. A new spectrum between senescence and apoptosis pathways. *Journal of Investigative Dermatology* DOI: <http://dx.doi.org/10.1016/j.jid.2016.09.014>
- (9) Estruch R, Ros E, Salas-Salvadó J, *et al.* Primary Prevention of Cardiovascular Disease with a Mediterranean Diet. *The New England Journal of Medicine.* Published online February 25 2013

Jenny Hall:

¹ Dienne J. Bosa, Simone J.T. van Montfort, Bob Oranje, Sarah Durston, Paul A.M. Smeets. Effects of omega-3 polyunsaturated fatty acids on human brain morphology and function: What is the evidence? *European Neuropsychopharmacology* (2016) 26, 546–561.

¹ I. Denis, B. Potier, S. Vancassel, C. Heberdena, M. Lavielle. Omega-3 fatty acids and brain resistance to ageing and stress: Body of evidence and possible mechanisms. *Ageing Research Reviews* 12 (2013) 579–594.

¹ Davidovic M, Sevo G, Svorcan P, Milosevic DP, Despotovic N, Erceg P. Old age as a privilege of the “selfish ones.” *Aging and Disease*. 2010;1(2):139-146.

¹ Simmons, D. (2008) Epigenetic influence and disease. *Nature Education* 1(1):6.

¹ Gemma C, Vila J, Bachstetter A, Bickford PC. Oxidative Stress and the Aging Brain: From Theory to Prevention. In: Riddle DR, editor. *Brain Aging: Models, Methods, and Mechanisms*. Boca Raton (FL): CRC Press/Taylor & Francis; 2007. Chapter 15.

¹ Tosato M, Zamboni V, Ferrini A, Cesari M. The aging process and potential interventions to extend life expectancy. *Clinical Interventions in Aging*. 2007;2(3):401-412.

¹ Franceschi C, Bonafè M, Valensin S, Olivieri F, De Luca M, Ottaviani E, De Benedictis G. Inflamm-aging. An evolutionary perspective on immunosenescence. *Ann N Y Acad Sci*. 2000 Jun;908:244-54.

Ask the experts:

Natalie Lamb:

1. Jones ML, Martoni CJ, Prakash S. Oral Supplementation With Probiotic *L. reuteri* NCIMB 30242 Increases Mean Circulating 25-Hydroxyvitamin D: A Post Hoc Analysis of a Randomized Controlled Trial. *J Clin Endocrinol Metab* 2013; **98**(7):2944-51.
2. Vighi G, Marcucci F, Sensi L, Di Cara G, Frati F. Allergy and the gastrointestinal system. *Clin Exp Immunol* 2008; **153** Suppl 1:3-6.
3. de Vrese M, Winkler P, Rautenberg P, Harder T, Noah C, Laue C, Ott S, Hampe J, Schreiber S, Heller K, Schrezenmeir J. 2005. Effect of *Lactobacillus gasseri* PA 16/8, *Bifidobacterium longum* SP 07/3, *B. bifidum* MF 20/5 on common cold episodes: a double blind, randomized, controlled trial. *Clin Nutr*. Aug;**24**(4):481-91.
4. Lutgendorff F, Akkermans LM, Soderholm JD. The Role of Microbiota and Probiotics in Stress-induced Gastro-intestinal Damage. *Current Molecular Medicine* 2008;**8**: 282-298.

Julie Lamble:

- (1) *International Journal of Food Sciences and Nutrition* Vol. 67 (2016)
- (2) *EFSA Journal* 2010; 8 (10) 1798