



Valerian Root and Lemon Balm Extracts

A Phytomedicine Compound Improves Symptoms of Hyperactivity, Attention Deficits, and Impulsivity in Children

■ *Stephanie Maxine Ross, MHD, MS, HT, CNC, PDMT*

Holist Nurs Pract 2015;29(6):391–395

One of the most common childhood behavior disorders presently diagnosed in children is attention-deficit/hyperactivity disorder (ADHD) and therefore represents an important public health concern.¹ This neurobehavioral disorder is characterized by developmental inappropriate levels of hyperactivity, attention deficits, and impulsivity that result in functional impairment on several levels, including academic performance, family and peer relationships, and cognitive deficits.^{2,3} Several reports document an ever-increasing trend both in the prevalence of ADHD and in the use of ADHD medications over the past decade.⁴

A study by the Food and Drug Administration indicates that prescription medications for childhood ADHD increased by 48% between 2002 and 2010.⁵ During this same time period, the Centers for Disease Control and Prevention estimated that the number of

Phytomedicine improves symptoms of hyperactivity, attention deficits, and impulsivity in children.

children aged 3 to 17 years with an ADHD diagnosis increased from 4.4 million to 5 million.⁶

Current available treatments focus on the reduction of ADHD symptoms and improving functioning. The most common pharmacological intervention for treatment of ADHD is psychostimulants, which have shown beneficial effects in short-term randomized studies. Although pharmaceutical drugs have shown to improve ADHD symptoms, they are often

associated with adverse effects, such as insomnia, decreased appetite, irritability, and impaired growth.⁷⁻⁹ For this reason, many parents prefer more natural treatment therapies for the management of ADHD symptoms in their children. This seems to be a shared consensus in the United States, Canada, and in other parts of the world.¹⁰⁻¹⁵ Statistics show that approximately 7% to 64% of children with a diagnosis of ADHD are treated with various natural therapeutic approaches.¹⁶⁻²⁰

Author Affiliation: College of Nursing and Health Professions, Drexel University, Philadelphia, Pennsylvania.

The author has disclosed that she has no significant relationships with, or financial interest in, any commercial companies pertaining to this article.

Correspondence: Stephanie Maxine Ross, MHD, MS, HT, CNC, PDMT, Associate Science Editor, Director and Clinical Assistant Professor, Advanced Study in Complementary and Integrative Health Programs, College of Nursing and Health Professions, Drexel University, 1505 Race St, Philadelphia, PA19102 (smr49@drexel.edu).

DOI: 10.1097/HNP.000000000000118

HYPERACTIVITY, ATTENTION DEFICITS, AND IMPULSIVITY

Treatment of subclinical symptoms

According to the Centers for Disease Control and Prevention, current statistics indicate that approximately 11% of children, aged 4 to 17 years (6.4 million), have received a diagnosis of ADHD as

of 2011.²¹ The percentage of children with an ADHD diagnosis increased from 7.8% in 2003 to 9.5% in 2007 and 11% in 2011. Rates of ADHD diagnosis increased an average of 3% per year from 1997 to 2006 and an average of approximately 5% per year from 2003 to 2011.²¹ Yet, these statistics represent only the percentage of children who met the criteria for ADHD diagnosis according to the *Diagnostic and Statistical Manual of Mental Disorders* (Fourth Edition) (*DSM-IV*), without any consideration for those children who suffer from hyperactivity, attention deficits, and impulsive behaviors either as single symptoms or symptoms combinations of milder or fluctuating intensity.²²

As previously noted, various natural therapeutic approaches are used in children with a diagnosis of ADHD in lieu of pharmaceutical drugs. For children suffering from subclinical symptoms, complementary and integrative health interventions become increasingly viable. These alternatives include phytomedicines that have shown efficacy and excellent tolerability in children younger than 12 years, experiencing restlessness and insomnia. These phytomedicines include valerian (*Valeriana officinalis*), which has shown to improve sleep disturbances in both adults and children,^{23,24} and lemon balm (*Melissa officinalis*), which is used to promote relaxation and restful sleep and to increase attention.^{25,26}

PHYTOMEDICINE PROFILE

Valerian (*Valeriana officinalis* L.)²⁷

Valeriana officinalis L. (Fam: Valerianaceae) is a perennial herb native to Europe and Asia and naturalized in North America. The plant grows in rich, moist soil and is characterized by yellow-brown rhizomes (underground stems), dark green pinnately compound leaves, and hollow stems that are crowned with clusters of white or pink flowers.

Valerian has a long-established historical reference of use both as a mild sedative and as a sleep aid in Western Europe. The Greek physician Hippocrates recommended its medicinal properties in the fourth-century BC, primarily for digestive disorders, nausea, and menstrual cramps.²⁸ However, it was the Greek physician Galen who first recorded valerian's sleep-promoting properties in 2 AD.^{29,30} In medieval Europe, valerian was used as a tranquilizing agent to treat epilepsy. By the late 16th century, the medicinal

properties of valerian were used for the treatment of insomnia, anxiety, and nervous afflictions such as nervous digestive upset.³¹

In 1620, the English colonists brought valerian roots and other medicinal plants to North America. During the 1700s to the mid-1900s, valerian was esteemed as a sedative, as a remedy for nervous disorders, and as a treatment option for sleeplessness. It was recognized as an official remedy in the United States Pharmacopoeia from 1820 to 1936 and was included in the National Formulary from 1888 to 1946. Today, the valerian (*Valeriana officinalis*) root extract is an approved over-the-counter medicine in Germany, Switzerland, Belgium, Italy, and France for the treatment of stress and nervous tension, disturbed sleep patterns, and anxiety states. In Germany, the valerian root extract is an approved herbal medicine listed in the German Commission E monographs for its sedative and sleep-promoting activity.

Phytochemistry and phytopharmacology

Valerian consists of more than 150 known chemical constituents, many of which have been demonstrated to be physiologically active; yet, it is unclear as to which of the chemical constituents is responsible for its sleep-promoting effects. In fact, scientists believe that its pharmacological activity may result from interactions among multiple constituents rather than any one compound or class of compounds. The primary active constituents include valerian's essential oil and its corresponding sesquiterpenes (valerenic acid), the iridoid esters (valepotriates), amino acids (γ -amino butyric acid [GABA], tyrosine, glutamine), and alkaloids.^{32,33}

The exact pharmacological mechanism for valerian's relaxation effects has yet to be determined. In pharmacological studies, valepotriate constituents have demonstrated sedative and spasmolytic effects and the sesquiterpenes and valerenic acid have been shown to cause sedation.^{34,35} Valerenic acid and other constituents of valerian have been found to be GABA agonists. Several theories have been proposed to explain valerian's mechanism of action. It is possible that valerian constituents may inhibit the enzyme system responsible for the central catabolism of GABA, increasing GABA concentrations, and decreasing central nervous system activity. Valerian may also bind directly to GABA type A receptors and stimulate the release and reuptake of GABA.³⁶

PHYTOMEDICINE PROFILE

Lemon balm (*Melissa officinalis* L.)

Melissa officinalis L. (Fam: Lamiaceae) is a perennial, lemon-scented, aromatic herb that is characterized by serrated, heart-shaped leaves that attach to square, branching stems. It has been cultivated around the Mediterranean coast for more than 2000 years for its many healing properties and enjoys a long history of use as a sedative, antispasmodic, and antibacterial. The genus name, *Melissa*, is derived from the Greek word for “bee” due to the plants reputed ability to attract honeybees to its flower and the quality of honey produced from it. The species name, *officinalis*, is an epithet meaning “used in medicine,” indicating that the species has historic medicinal uses. The common name lemon balm originates from the Greek word *balsamon*, which translated means balsam, or “an oily, sweet-smelling resin.”³⁷

Throughout history, lemon balm has been used medicinally to heal wounds, prevent and treat cold sores, soothe nerves, improve sleep, and strengthen the memory and the mind. The ancients are known to steep lemon balm in wine, a traditional medicinal dosage form, for fevers and to uplift the spirits. Its medicinal properties were recorded as early as 300 BC in Theophrastus’s *Historia Plantarum* and the Greek physician Dioscorides’ *De Materia Medica* (50-80 BC). Avicenna, a Muslim physician and philosopher (980-1037 AD), prescribed lemon balm for wounds and ulcers. Medicinal use throughout this early epoch include a recommendation by the 16th-century physician Paracelsus, who thought *Melissa* so potent that it would revivify patients close to death and prescribed lemon balm for “all complaints supposed to proceed from a disordered state of the nervous system.”^{28(p825)} Antiquarian herbal pharmacopeias also attributed balm tea (infusion) for its beneficial effects on the brain, including its memory-improving properties, more recently corroborated as cholinergic binding activities identified in lemon balm extracts.^{38,39} Today, *Melissa officinalis* is recognized for its sedative effects, with indications encompassing nervous disorders, including reduction of anxiety and stress, excitability, sleep disturbance, and gastrointestinal disorders.²⁹

Phytochemistry and phytopharmacology

Lemon balm’s medicinal properties are derived from the leaf and its aromatic components or volatile oils.

Lemon balm contains more than 100 chemicals including the flavonoids (quercitrin and rhamnocitrin), which have an antioxidant effect; phenolic acids and tannins, primarily rosmarinic acid, which are astringent and contribute to lemon balm’s antiviral effect; the 7-glucosides (apigenin, kaempferol, quercetin, and luteolin); caffeic and chlorogenic acids; triterpenes; and volatile oils citral a, citral b, (10%-30%), and citronellal (30%-40%) that render its lemony flavor and aroma.

For children experiencing mild or varying levels of intensity in hyperactivity, attention deficits, or impulsivity and who do not meet the criteria for ADHD according to the *DSM-IV*, complementary and integrative health interventions, such as phytomedicines, become increasingly viable. In clinical studies, it has been demonstrated that valerian (*Valeriana officinalis*) and lemon balm (*Melissa officinalis*) help reduce the incidence of insomnia and restlessness. In one multicenter study, the purpose was to evaluate the effectiveness of a fixed combination valerian and lemon balm preparation for children with subclinical ADHD symptoms.

RESEARCH IN REVIEW

In a prospective, multicenter, open-label study, the efficacy and tolerability of a fixed combination valerian (*Valeriana officinalis*) root extract and lemon balm (*Melissa officinalis*) aerial extract was evaluated in primary school children experiencing hyperactivity, attention deficits, and impulsiveness but did not meet the criteria for ADHD according to the *DSM-IV*.⁴⁰

Study design

This prospective, multicenter, observational study was conducted in 27 pediatrician practices located throughout Germany. The inclusion population consisted of 169 primary school children, aged 6 to 11 years, experiencing various levels of hyperactivity, attention deficits, and impulsiveness but not meeting the diagnostic criteria for ADHD according to the *DSM-IV* and therefore not candidates for receiving conventional drug therapy. Patients with contraindications to the test agent phytomedicine were excluded from the study. Patients were instructed to take 2 coated tablets of the fixed combination phytomedicine Sandrin (Dr Willmar Schwabe GmbH & Co KG, Karlsruhe, Germany), 2 times per day, for

the 7-week duration of the study. The daily dosage of the fixed combination test agent (Sandrin) contained 640 mg/d of the quantified dry extract WS 1014 from valerian root (drug/extract ratio 3-6:1, solvent ethanol 62% [m/m] and 320 mg of the quantified lemon balm dry extract WS 1303 [drug/extract ratio 4-6:1, solvent ethanol 30% [m/m]). The treatment period was a total of 7 weeks, with examinations at baseline, after 2 weeks, and at the end of the 7th week.

The attending pediatricians rated the patients' behavioral symptoms using the Likert scales ranging from 0 (*not present*) to 5 (*very strong*) over the past 7 days with respect to the following symptoms: concentration problems, hyperactivity, impulsiveness, impaired social behavior, difficulties falling asleep, or sleeping through the night and morning fatigue. At subsequent examinations, symptoms, changes in therapy, compliance, and any adverse reactions to the test agent were recorded. In addition, the parents completed a questionnaire assessing their child's behavior in the last 7 days at every visit with regard to attention deficits, nervousness, hyperactivity, impulsiveness, anxiety, and behavior for both school and family environments. Statistical analysis was descriptive and explorative. Upon final examination, the pediatrician and parents provided a global assessment of efficacy and tolerability.

Observations and results

At the onset of the study, pediatricians reported that dominating symptoms among patients were pronounced attention deficits, hyperactivity, and impulsiveness, followed by impaired social behavior; sleep disturbances and morning fatigue were less prominent. Under the fixed combination phytomedicine treatment, all symptoms improved considerably ($P < .0001$). The parents' ratings of symptom severity decreased from a mean overall score of 3.2 at baseline to 2.7 at the end of the study. More specifically, there was a significant improvement compared with baseline in the following areas: problems with friends and leisure time, difficulties in everyday life, burden on child, burden on parents and family, and problems in school ($P < .0001$).

At baseline, 58% of the parents described their child's behavior as a heavy or very heavy burden, which decreased to 18% after 7 weeks of treatment. The symptom with the highest severity score at baseline was distractibility, which significantly decreased after 7 weeks of treatment ($P < .0001$).

SUMMARY OF RESULTS

Researchers found that primary school children with hyperactivity, attention deficits, and impulsiveness, but not meeting the diagnostic criteria for ADHD according to the DSM-IV, respond positively to 7 weeks of treatment with the combination valerian and lemon balm extract (Sandrin), with decreased incidence of overall symptoms and a reduction in problems in school and in the home environment.

The combined valerian and lemon balm phytomedicine extract provides a viable treatment option, in addition to nutritional and lifestyle modifications and professional counseling.

AUTHOR COMMENTS

Attention-deficit/hyperactivity disorder is recognized as a complex multifactorial condition. In light of the apparent increase in the number of children with a diagnosis of ADHD, and for those children who suffer from hyperactivity, attention deficits, and impulsive behaviors either as single symptoms or symptoms combinations of milder or fluctuating intensity, there is an apparent need both to identify the underlying causative factors and to apply a holistic, complementary, and integrative approach to restore balance and function.

REFERENCES

1. Jensen PS, Hinshaw SP, Swanson JM, et al. Findings from the NIMH multimodal treatment study of ADHD (MTA): implications and applications for primary care providers. *J Dev Behav Pediatr*. 2001;22:60-73.
2. American Psychiatric Association. *Diagnostic and Statistical Manual of Mental Disorders: DSM-IV-TR*. Washington, DC: American Psychiatric Association; 2000.
3. Rasmussen P, Gillberg C. Natural outcome of ADHD with developmental coordination disorder at age 22 years: a controlled, longitudinal, community-based study. *J Am Acad Child Adolesc Psychiatry*. 2000;39:1424-1431.
4. Pastor PN, Reuben CA. Diagnosed attention deficit hyperactivity disorder and learning disability: United States, 2004-2006. *Vital Health Stat*. 2008;10:237.
5. Grace C, Governale L, McMahon A, Trinidad J, Staffa J, Murphy D. Trends of outpatient prescription drug utilization in US children, 2002-2010 Online Pediatrics. <http://www.aappublications.org/content/130/1/23>. Accessed August 8, 2015.
6. Centers for Disease Control and Prevention. Prevalence of attention deficit hyperactivity disorder: United States, 2002-2010. <http://www.cdc.gov/mmwr/preview/mmwrhtml/mm5944a3.htm>. Accessed August 8, 2015.
7. MTA Cooperative Group. National Institute of Mental Health Multimodal Treatment Study of ADHD follow-up: 24-month outcomes of treatment strategies for attention-deficit/hyperactivity disorder. *Pediatrics*. 2004;113:754-761.

8. MTA Cooperative Group. National Institute of Mental Health Multimodal Treatment Study of ADHD follow-up: changes in effectiveness and growth after the end of treatment. *Pediatrics*. 2004; 113:762-769.
9. Charach A, Ickowicz A, Schachar R. Stimulant treatment over five years: adherence, effectiveness, and adverse effects. *J Am Acad Child Adolesc Psychiatry*. 2004;43:559-567.
10. Spiegelblatt L, Laine-Ammara G, Pless IB, Guyver A. The use of alternative medicine by children. *Pediatrics*. 1994;94:811-814.
11. American Academy of Pediatrics, Committee on Children With Disabilities. Counseling families who choose complementary and alternative medicine for their child with chronic illness or disability. *Pediatrics*. 2001;107:598-601.
12. Baumgaertel A. Alternative and controversial treatments for attention-deficit/hyperactivity disorder. *Pediatr Clin North Am*. 1999;46:977-992.
13. Chan E, Rappaport LA, Kemper KJ. Complementary and alternative therapies in childhood attention and hyperactivity problems. *J Dev Behav Pediatr*. 2003;24:4-8.
14. Kemper KJ. Dietary supplements for attention-deficit/hyperactivity disorder—a fishy business? *J Pediatr*. 2001;139:173-174.
15. Gross-Tsur V, Lahad A, Shalev RS. Use of complementary medicine in children with attention deficit hyperactivity disorder and epilepsy. *Pediatr Neurol*. 2003;29:53-55.
16. Fuchs T, Birbaumer N, Lutzenberger W, Gruzelier JH, Kaiser J. Neurofeedback treatment for attention-deficit/hyperactivity disorder in children: a comparison with methylphenidate. *Appl Psychophysiol Biofeedback*. 2003;28:1-12.
17. Heywood C, Beale I. EEG biofeedback vs placebo treatment for attention deficit/hyperactivity disorder: a pilot study. *J Atten Disord*. 2003;7:43-55.
18. Lubar JF, Swartwood MO, Swartwood JN, O'Donnell PH. Evaluation of the effectiveness of EEG neurofeedback training for ADHD in a clinical setting as measured by changes in T.O.V.A. scores, behavioral ratings, and WISC-R performance. *Biofeedback Self Regul*. 1995;20: 83-99.
19. Nash JK. Treatment of attention deficit hyperactivity disorder with neurotherapy. *Clin Electroencephalogr*. 2000;31:30-37.
20. Stevens L, Zhang W, Peck L, et al. EFA supplementation in children with inattention, hyperactivity, and other disruptive behaviors. *Lipids*. 2003;38:1007-1021.
21. Centers for Disease Control and Prevention. Attention-deficit hyperactivity disorder (ADHD): data & statistics. <http://www.cdc.gov/ncbddd/adhd/data.html>. Accessed August 8, 2015.
22. American Psychiatric Association. *Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition: DSM-5*. Washington, DC: American Psychiatric Association; 2013.
23. Fernandez-San-Martin MI, Masa-Font R, Palacios-Soler L, Sanchez-Gomez P, Calbo-Caldentey C, Flores-Mateo G. Effectiveness of valerian on insomnia: a meta-analysis of randomized placebo-controlled trials. *Sleep Med*. 2010;11:505-511.
24. Francis AJ, Dempster RJ. Effect of valerian, *Valeriana edulis*, on sleep difficulties in children with intellectual deficits: randomized trial. *Phytomedicine*. 2002;9:273-279.
25. Kennedy DO, Sholey AB, Tildesley NT, Perry EK, Wesnes KA. Modulation of mood and cognitive performance following acute administration of *Melissa officinalis* (lemon balm). *Pharmacol Biochem Behav*. 2002;72:953-964.
26. Kennedy DO, Little W, Sholey AB. Attenuation of laboratory-induced stress in humans after acute administration of *Melissa officinalis* (Lemon Balm). *Psychosom Med*. 2004;66:607-613.
27. Ross SM. Psychophytomedicine: an overview of clinical efficacy and phytopharmacology for treatment of depression, anxiety and insomnia. *Holist Nurs Pract*. 2014;28(4):275-280.
28. Grieve M. *A Modern Herbal*. Vol 2. New York, NY: Hafner Press; 1974:824-830.
29. Blumenthal M, Goldberg A, Brinckmann J. *Herbal Medicine Expanded Commission E Monographs*. Newton, MA: Integrative Medicine Communications; 2000:394-400.
30. Turner W. *A New Herbal, Parts II and III*. Cambridge, England: Cambridge University Press; 1995:464-466.
31. Culpeper N. Garden valerian. In: *Culpeper's Complete Herbal*. New York, NY: W Foulsham; 1994:295-297.
32. Russo EB. *Handbook of Psychotropic Herbs: A Scientific Analysis of Herbal Remedies in Psychiatric Conditions*. Binghamton, NY: Haworth Press; 2001:95-106.
33. Houghton PJ. The scientific basis for the reputed activity of valerian. *J Pharm Pharmacol*. 1999;51:505-512.
34. Newall C, Anderson L, Phillipson J. *Herbal Medicines: A Guide for Healthcare Professionals*. London, England: Pharmaceutical Press; 1996:260-262.
35. Plushner SL. Valerian: *Valeriana officinalis*. *Am J Health Syst Pharm*. 2000;57:328-332.
36. Lefebvre T, Foster BC, Drouin CE, Krantis A, Livesey JF, Jordan SA. In vitro activity of commercial valerian root extracts against human cytochrome P450 3A4. *J Pharm Pharm Sci*. 2004;7:265-273.
37. Dobelis IN, ed. *Magic and Medicine of Plants*. Pleasantville, NY: The Reader's Digest Association Inc; 1986:37-43.
38. Perry EK, Pickering AT, Wang WW, Houghton PJ, Perry NL. Medicinal plants and Alzheimer's disease; from ethnobotany to phytotherapy. *J Pharm Pharmacol*. 1999;51:527-534.
39. LeStrange RA. *History of Herbal Plants*. London, England: Morrison & Gibb; 1997:25-26.
40. Gromball J, Beschoner F, Wantzen C, Paulsen U, Burkart M. Hyperactivity, concentration difficulties and impulsiveness improve during seven weeks' treatment with valerian root and lemon balm extracts in primary school children. *Phytomedicine*. 2014;21:1098-1103.