

## Select Herbs Targeted to Eradicating Gastrointestinal Dysbiosis.

By: Rachel Olivier, MS, ND, PhD

Dysbiosis is the classic term for an imbalance of gastrointestinal microflora, indicating an increase in abnormal or noncommensal flora, with a coinciding decrease in commensal or normal flora. An increase in pathogenic bacteria, including *Shigella flexneri* and *Salmonella enteritidis*, opportunistic bacteria, including *Klebsiella pneumoniae*, *Escherichia coli*, *Pseudomonas aeruginosa*, *Staphylococcus aureus*, and *Clostridium difficile*, and yeasts, including *Candida albicans* in the lower bowel is typically associated with dysbiosis.<sup>1</sup> In addition to the intestinal tract, dysbiosis of the mouth is also known to occur, and is associated with dental carries.<sup>2</sup> There are numerous factors correlated with dysbiosis, including a poor diet, physical and/or psychological stress, and the overuse of antibiotics, which in turn results in depressed immunity. Psychological stress has been demonstrated to decrease the level of secretory IgA, resulting in decreased mucosal immunity.<sup>3</sup> In addition to other coinciding factors, intestinal dysbiosis has been implicated as the root cause of bowel inflammation.<sup>4</sup> The root cause of many chronic degenerative diseases is correlated to the health of the bowel; consequently optimizing bowel health offers a significant advantage for long lasting health benefits.

Select herbs are well recognized in promoting the synergistic healing of damaged intestinal tissue, resulting predominately from dysbiosis. These herbs include:

***Stemona sessilifolia*** (root) - The active principals of *Stemona* are its alkaloids. These alkaloids exert antifungal, antibacterial and pesticidic properties. It is typically indicated for acute and chronic cough; cough in phthisis (wasting syndrome), whooping cough, cough occurring with or after the common cold, and for cough due to exopathogens. Its action is said to be warm in nature, rather than dry, and its use is considered calming to the entire respiratory center. It also has proven effectiveness for the eradication of louse, parasites,<sup>5</sup> and worms (pinworms).<sup>6, 7, 8</sup>

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<sup>1</sup> Kirillov DA, Chaĭnikova IN, Perunova NB, Chelpachenko OE, Pan'kov AS, Smoliagin AI, Valyshev AV. [Effect of a polyoxydonium immunoregulator on the biological properties of microorganisms]. [Article in Russian]. Zh Mikrobiol Epidemiol Immunobiol. 2003 Jul-Aug;(4):74-8.

<sup>2</sup> Davydova TR, Karasenkova IaN, Khavkina Elu. [The problem of dysbiosis in practical dentistry]. [Article in Russian]. Stomatologiya (Mosk). 2001;80(2):23-4.

<sup>3</sup> Drummond PD, Hewson-Bower B. Increased psychosocial stress and decreased mucosal immunity in children with recurrent upper respiratory tract infections. J Psychosom Res. 1997;43:271-278.

<sup>4</sup> McKay DM. Intestinal inflammation and the gut microflora. Can J Gastroenterol. 1999 Jul-Aug; 13(6):509-16.

<sup>5</sup> Herbasin Chinese herb database, <http://www.herbasin.com/database/baibu.htm>.

<sup>6</sup> Pharmacopoeia Commission of the People's Republic of China. **Pharmacopoeia of the People's Republic of China**, English Ed, Volume I. Chemical Industry Press, Beijing, 1997, p 173.

<sup>7</sup> Chang HM, But PP. **Pharmacology and Applications of Chinese Materia Medica**. Volume I. World Scientific, Singapore. 1987, pp 484-488.

<sup>8</sup> Bensky D, Gamble A. **Chinese Herbal Medicine Materia Medica**. Eastland Press, Seattle, 1986, pp 297-298.

***Artemisia absinthium*, Wormwood** (shoots, leaves) – In Traditional Chinese Medicine (TCM) *Artemisia* has been used as an antiparasitic agent for more than 1,000 years,<sup>9</sup> as well as an anthelmintic since primordial times. Its parasitic properties are attributed partially to its  $\alpha$ -santonin content.<sup>10</sup> It is also regarded as a potent and rapidly acting antimalarial herb.<sup>11, 12</sup> Its primary actions are noted to include cholagogue (inducing bile flow), digestive, appetite stimulating and wound healing, of which all are attributed to its essential oils and amaroids.<sup>13</sup> Following ingestion, the artemisinins are rapidly absorbed and subsequently penetrate the blood-brain barrier, and as in the case of malaria, accumulate into parasite infected erythrocytes. In turn these parasite infected erythrocytes are phagocytized by the leukocytes, thus subsequently eliminated.

In addition to its antiparasitic properties, the essential oil also possesses antimicrobial activity. *In vitro*, its use has been demonstrated to retard the growth of the parasite *Plasmodium falciparum*,<sup>14</sup> and has a confirmed 94.5% success rate in hookworm eradication.<sup>13</sup> It has also been demonstrated to exhibit hepatoprotective activities, partially via its inhibition of microsomal drug metabolizing enzymes (MDME).<sup>15</sup>

*Artemisia* intake has also been demonstrated to have an action in the stimulation the bitter receptors in the taste buds of the tongue, which in turn triggers a reflexive increase in stomach acid secretion. With intake a significant increase in the production of alpha-amylase, lipase, and other digestive secretions has been demonstrated.<sup>16</sup> Bitter taste receptor activation has been associated with a rapid change in the level of second messengers. Recent research has correlated the ingestion of bitter stimuli with an initiation of both a cellular and molecular responses in the endocrine cells of the GI tract, postulating that “some elements of taste-specific signaling are operative in enteroendocrine cells.”<sup>17</sup>

***Brucea javanica* (fruit)** – The active constituents of *Brucea javanica* are the quassinoid compounds bruceantin and brucein C.<sup>18</sup> It possesses properties designated as beneficial

<sup>9</sup> Van Boxel CJ. *Artemisia* and Artemisinin, a story about toxicity. UPPSALA Reports 25. April 2004.

<sup>10</sup> Perez-Souto N, Lynch RJ, Measures G, Hann JT. Use of high-performance liquid chromatographic peak deconvolution and peak labeling to identify antiparasitic components in plant extracts. *J Chromatography*. 1995 593:209-215.

<sup>11</sup> Chanphen R, Thebtaranonth Y, Wanauppathamkul S, Yuthavong Y. Antimalarial Principles from *Artemisia indica*. *J. Nat. Prod.*, 1998, 61 (9), pp 1146–1147.

<sup>12</sup> World Health Organization. The use of antimalarial drugs. Report of a WHO Technical Consultation. World Health Organization, Geneva, Switzerland 2001 (document WHO/CDS/RBM/33).

<sup>13</sup> **PDR for Herbal Medicines**. 2<sup>nd</sup> Edition. 2000 Medical Economics Company, Inc. Montvale, NJ.

<sup>14</sup> Hernandez H, Mendiola J, Torres D, Garrido N. Effect of aqueous extracts of *Artemisia* on the *in vitro* culture of *Plasmodium falciparum*. *Fitoterapia* 1990 61(6):540-541.

<sup>15</sup> Gilania H A-U, Janbaz KH. Preventive and Curative Effects of *Artemisia absinthium* on Acetaminophen and CCl<sub>4</sub>-induced Hepatotoxicity. *General Pharmacology*. 1995 26(2):309-315.

<sup>16</sup> Chevallier. A. **The Encyclopedia of Medicinal Plants**. Dorling Kindersley. London 1996 ISBN 9-780751-303148.

<sup>17</sup> Rozengurt E. Taste receptors in the gastrointestinal tract. I. Bitter taste receptors and alpha-gustducin in the mammalian gut. *Am J Physiol Gastrointest Liver Physiol*. 2006 Aug;291(2):G171-7. Epub 2006 May 18.

<sup>18</sup> Keene AT et al. *In vitro* amoebicidal testing of natural products, Part I. Methodology. *Planta medica*. 1986 52:278–285.

to multiple bodily systems, including the digestive and circulatory systems, and the large intestines. Both the roots and fruits of *Brucea javanica* are used as popular agents against diarrhea, dysentery and fever.<sup>19</sup> *In vitro* studies have verified that *Brucea javanica* extracts are effective as amoebicides,<sup>20</sup> and clinical studies have shown it to be an effective agent in the treatment of amoebic dysentery<sup>21, 22</sup> and malaria.<sup>23</sup> In animal studies *B. javanica* has been demonstrated to play a role in immunological regulation, as evidenced by its killing effect on the cysts associated with *Pneumocystis carinii* pneumonia.<sup>24</sup> Other reports have illustrated its activity against various non-commensal organisms including *Shigella* species (*S. shiga*, *S. flexneri*, *S. boydii*), *Salmonella* species (*S. lexington*, *S. derby*, *S. typhi* type II) and *Vibrio* species (*V. cholerae*, *V. inaba* and *V. cholerae ogawa*).<sup>25</sup>

***Pulsatilla chinensis*** (rhizome) – The root (rhizome) of *Pulsatilla chinensis* has been described as possessing anodyne (pain relieving), anti-inflammatory, antispasmodic, astringent and sedative properties.<sup>26, 27, 28</sup> It is noted as an effective agent for bacterial and amoebic dysentery,<sup>27, 28</sup> and is traditionally used in the treatment of malaria, nose bleeds and hemorrhoids, as well as externally to treat infestation with *Trichomonas vaginitis*.<sup>27, 16</sup> It is also thought to clear toxicity and lower fever.<sup>29</sup> The active compound in the root is the lactone protoanemonin, which is recognized as the bactericidal agent.<sup>16</sup>

***Picrasma excelsa*** (bark) – Also referred to as Quassia, this herb is considered a powerful simple bitter, hence its use as a digestive aide. The two main ingredients are quassin and neoquassin. Traditional use is as a remedy for roundworms, as an insecticide, and as a remedy for headlice. It is also used as a remedy for digestive disorders, and for parasites.<sup>30</sup> Orally it is used for anorexia, indigestion, constipation, fever, or as an anthelmintic for thread worms, nematodes, and ascaris.<sup>31</sup> A recent study with *P. excelsa*

<sup>19</sup> [http://www.asianplant.net/Simaroubaceae/Brucea\\_javanica.htm](http://www.asianplant.net/Simaroubaceae/Brucea_javanica.htm)

<sup>20</sup> WHO Monographs on Selected Medicinal Plants. Volume 1. WHO Library Cataloguing in Publication Data. 1999.

<sup>21</sup> Tang W, Eisenbrand G. Chinese drugs of plant origin, chemistry, pharmacology and use in traditional and modern medicine. Berlin, Springer-Verlag, 1992:207–222.

<sup>22</sup> Steak EA. The chemotherapy of protozoan diseases, Vol. 1. Washington, DC, US Government Printing Office, 1972.

<sup>23</sup> O'Neill MJ, Bray DH, Boardman P, Chan KL, Phillipson JD, Warhurst DC, Peters W. Plants as Sources of Antimalarial Drugs, Part 4: Activity of *Brucea javanica* Fruits Against Chloroquine-Resistant *Plasmodium falciparum* in vitro and Against *Plasmodium berghei* in vivo. *J. Nat. Prod.* 1987 50 (1):41–48.

<sup>24</sup> Abstract by: TsingHua. Author: Unknown. Immunological Regulation and Treatment of *Brucea javanica* and *Fructus Psoraleae* on Rats with *Pneumoc.* Chinese Journal of Parasitology and Parasitic Diseases. 2007.

<sup>25</sup> Wasuwat S et al. Study on antidyentery and antidiarrheal properties of extracts of *Brucea amarissima*. Bangkok, Applied Science Research Center of Thailand, 1971:14 (Research Project Report 17/10, 2).

<sup>26</sup> Kariyone. T. *Atlas of Medicinal Plants*. Osaka: Takeda Chemical Industries; 1971.

<sup>27</sup> Yeung H-C. Handbook of Chinese Herbs and Formulas. Institute of Chinese Medicine, Los Angeles 1985.

<sup>28</sup> Duke JA, Ayensu ES. *Medicinal Plants of China*. Reference Publications, Inc. 1985 ISBN 0-917256-20-4.

<sup>29</sup> [http://www.ibiblio.org/pfaf/cgi-bin/arr\\_html?Pulsatilla+chinensis](http://www.ibiblio.org/pfaf/cgi-bin/arr_html?Pulsatilla+chinensis)

<sup>30</sup> [http://www.naturalstandard.com/Picrasma\\_excelsa](http://www.naturalstandard.com/Picrasma_excelsa).

<sup>31</sup> <http://www.naturaldatabase.com/Quassia>

noted a moderate inhibition of the cytochrome P450 (CYP) enzyme 1A1. This enzyme is a known activator of carcinogens.<sup>32</sup>

***Acacia catechu*** (stem) – The herb *Acacia catechu* is typically utilized for its astringent and antioxidant properties. The catechins isolated from this herb have significant antioxidant and antimicrobial properties. In many parts of the world chewing sticks are made out of the stem, and because of its antimicrobial properties it is considered a valuable component for dental care.<sup>33</sup> The chief phytoconstituents of the heartwood are catechin and epicatechin.

***Hedyotis diffusa*** – *Hedyotis diffusa* is one of the most popular herbs used in traditional Chinese medicine (TCM). It has been demonstrated to possess antioxidant,<sup>34</sup> anti-inflammatory, hepatoprotective,<sup>35</sup> neuroprotective,<sup>36</sup> and antitumor properties.<sup>37</sup> Its active principles include anthraquinones,<sup>38, 39</sup> iridoid glucosides,<sup>36, 34</sup> triterpenoids,<sup>40</sup> and flavonoids.<sup>36, 34</sup>

**Yarrow (*Achillea millefolium*)** (leaf, flower) – The indications for the use of Yarrow, as approved by the German Commission E include loss of appetite, dyspeptic complaints and liver/gallbladder issues. The actions of its flavonoids are indicated as cholagogic (bile flow stimulant), and as a vitalizer in increasing the production of stomach acid. It also possesses both anti-edema and anti-inflammatory attributes.<sup>13</sup> Yarrow is recognized for its relaxant property on smooth muscles, thus may aid with the relief of stomach cramps<sup>41</sup> associated with dysbiosis. In one study utilizing Yarrow, an anti-Staphylococcal activity was demonstrated.<sup>42</sup>

**Dill (*Anethum graveolens*)**(seeds) – As a popular flavoring agent, dill has a history of use as an aromatic herb and spice exceeding 2000 years.<sup>43</sup> It is said to have a calming effect on both the autonomic nervous and digestive systems, as well as having

<sup>32</sup> Shields M, Niazi U, Badal S, Yee T, Sutcliffe MJ, Delgoda R. Inhibition of CYP1A1 by Quassinoids found in *Picrasma excelsa*. *Planta Med.* 2009 Feb;75(2):137-41. Epub 2008 Nov 18.

<sup>33</sup> <http://www.herbal-extract.org/>

<sup>34</sup> Lu CM, Yang JJ, Wang PY, Lin CC. *Planta Med.* 2000 66:374–377. doi: 10.1055/s-2000-8544.

<sup>35</sup> Lin CC, Ng LT, Yang JJ, Hsu YF. *Am J Chin Med.* 2002 30:225–234. doi:10.1142/S0192415X02000405.

<sup>36</sup> Kim Y, Park EJ, Kim J, Kim Y, Kim SR, Kim YY. *J Nat Prod.* 2001 64:75–78. doi: 10.1021/np000327d.

<sup>37</sup> Li R, Zhao HR, Lin YN. *J Chin Pharm Sci.* 2002 11:54–57.

<sup>38</sup> Ho TI, Chen GP, Lin YC, Lin YM, Chen FC. *Phytochem.* 1986 25:1988–1989. doi: 10.1016/S0031-9422(00)81192-9.

<sup>39</sup> Wu KS, Zhang K, Tan GS, Zeng GR, Zhou YJ. *Clin Pharm. J.* 2005 40:817–819.

<sup>40</sup> Lu HC, He J. *Nat Prod Res Dev.* 1996 8:34–37.

<sup>41</sup> <http://www.umm.edu>

<sup>42</sup> Molochko VA, Lastochkina TM, Krylov IA, Brangulis KA. [The antistaphylococcal properties of plant extracts in relation to their prospective use as therapeutic and prophylactic formulations for the skin] [Article in Russian] *Vestn Dermatol Venerol.* 1990;(8):54-6.

<sup>43</sup> Ishikawa TM, Kudo M, Kitajima J (2002). Water-soluble constituents of dill. *Chem. Pharm. Bull.* 55:501-507.

carminative and stomachic properties.<sup>44</sup> It is also indicated as a diuretic, antispasmodic and antibacterial agent, an expectorant, and as a pancreatic stimulant.<sup>45</sup>

The fruits (seeds) contain 1-4% essential oil, of which the primary compounds are corvone, limonene and  $\alpha$ -phellandrene, representing 30-60%, 33% and 21%, respectively.<sup>43, 46</sup> Potent antibacterial activity has been demonstrated with both aqueous and organic extracts of the seeds.<sup>47, 48, 49</sup> The compounds D-limonene and D-carvone, have been demonstrated to possess strong activity against the species *Aspergillus niger*, *Saccharomyces cerevisiae* and *Candida albicans*.<sup>50, 51, 52</sup> Its activity against both Gram negative and Gram positive bacteria, as well as fungi and molds has also been demonstrated.<sup>53</sup> Aside from its beneficial attributes towards eradicating these species, its primarily use is for the calming action it exerts on the digestive system, and as such aids in reducing gastrointestinal irritation.

By virtue of the combination of Eastern and Western herbs, the select botanicals discussed above afford a broad anti-dysbiotic effect, even with low dosing. In addition to providing an unfriendly environment for bowel pathogens, this combination of herbs is safe for continual use for up to eight weeks, as it has a low toxicity, and affords minimal irritation to the gut lining. By providing constituents to support the healing and maintenance of the digestive epithelial lining, as well as to eradicate non-commensal flora, the above mentioned herbals affords potent healing properties.

#### Cautions:

- Artemisia is not recommended concurrently with drugs that thin the blood, drugs that reduce stomach acid, or drugs that prevent or lessen seizures. Additionally, consumption may intensify the effects and side effects of alcohol.<sup>54</sup>
- Yarrow is contraindicated with blood thinners, particularly coumarin. As it contains simple coumarin components,<sup>55, 56</sup> it may interfere with anticoagulants and blood

<sup>44</sup> <http://nekkidrain.wordpress.com/>

<sup>45</sup> <http://www.essentialhealthandwellnesscentre.com>

<sup>46</sup> Raghavan S. **Handbook of spices, seasoning and flavourings**. 2nd edition. 2006 CRC Press Taylor and Francis group, Boca Raton, New York, pp 63-64, 104-105, 107-109.

<sup>47</sup> Arora DS, Kaur GJ. Antibacterial activity of some Indian medicinal plants. *J. Nat. Med.* 2007 61:313-317.

<sup>48</sup> Kaur GJ, Arora DS. In vitro antibacterial activity of three plants belonging to the family Umbelliferae. *Int. J. Antimicrob. Agents.* 2008 31:393-395.

<sup>49</sup> Kaur GJ, Arora DS. Antibacterial and phytochemical screening of *Anethum graveolens*, *Foeniculum vulgare* and *Trachyspermum ammi*. *BMC Complement. Altern. Med.* 2009 9:30.

<sup>50</sup> Delaquis PJ, Stanich K, Girard B, Mazza G. Antimicrobial activity of individual and mixed fractions of dill, cilantro, coriander and eucalyptus essential oils. *Int. J. Food Microbiol.* 2002 74:101-109.

<sup>51</sup> Jirovetz L, Buchbauer G, Stoyanova AS, Georgiev EV, Damianova ST. Composition, quality control and antimicrobial activity of the essential oil of long time stored dill (*Anethum graveolens* L.) seeds from Bulgaria. *J. Agric. Food Chem.* 2003 18:3854-3857.

<sup>52</sup> Stavri M, Gibbons S. The antimycobacterial constituents of Dill (*Anethum graveolens*). *Phytother. Res.* 2005 19: 938-941.

<sup>53</sup> Lopez P, Sanchez C, Battle R, Nerin C (2005). Solid and vapour phase antimicrobial activities of six essential oils: susceptibility of selected food-borne bacterial and fungal strains. *J. Agric. Food Chem.* 2005 53: 6939-6946.

<sup>54</sup> <http://www.drugdigest.org>

pressure medications. Additionally, yarrow may be contraindicated concurrently with the use of drugs that minimize or reduce the production of stomach acid.<sup>41</sup>

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<sup>55</sup> Hausen BM, Breuer J, Weglewski J, Rücker G. alpha-Peroxyachifolid and other new sensitizing sesquiterpene lactones from yarrow (*Achillea millefolium* L., Compositae). *Contact Dermatitis*. 1991 Apr;24(4):274-80.

<sup>56</sup> Final report on the safety assessment of Yarrow (*Achillea millefolium*) Extract. *Int J Toxicol*. 2001;20 Suppl 2:79-84.