

# Herbs for Herpes Simplex Infections

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Herpes simplex viruses (HSV) infect an extraordinary number of people. In one study looking at a large sample of the U.S. population from 1976 to 1994, 68% of the population 12 years and older had HSV-1 antibodies with little change during the period of the study.<sup>1</sup> Although HSV infections are rarely life threatening, they are associated with a high morbidity, and the rashes they cause are usually quite painful. Genital herpes ulcers may be a risk factor for transmission of human immunodeficiency virus (HIV).<sup>2</sup> In patients who develop severe immune suppression, HSV encephalitis can occur and is life threatening. Exposure of neonates to genital HSV can cause serious disease such as keratitis.<sup>3</sup> Though acyclovir and related drugs (famciclovir, valacyclovir) are now widely available to suppress HSV, cheap and effective natural prevention and treatment options are still sorely needed. This is particularly a concern as the risk of development of drug resistance exists with single-chemical agents. A recent study in The Netherlands, for example, found that 7% of immunocompromised patients had acyclovir-resistant HSV infections.<sup>4</sup> Clinical aspects of HSV and infections by these viruses are reviewed in the box, Clinical Review of Herpes Simplex.

## Mints Against Herpes

Various members of the Lamiaceae (mint) family of herbs offer safe and effective topical treatment for HSV outbreaks. The best-studied mint, *Melissa officinalis* (lemon balm), has

been shown to be effective as a concentrated extract in a cream base for relieving symptoms of acute herpes labialis in one open-controlled and three double-blind clinical trials.<sup>5-8</sup> The most recent and largest of these studies also found that prolonged use of the product increased the interval between acute outbreaks.<sup>7</sup> It has, unfortunately, not been tested directly in comparison to acyclovir or related drugs. What is clear is that, except for some generic brands of acyclovir from some suppliers, lemon balm cream is significantly less expensive.

Lemon balm leaf contains a variety of compounds that have shown anti-HSV activity in vitro. Earlier studies suggested that rosmarinic, caffeic, and ferulic acids were responsible for blocking activity of HSV-1.<sup>9</sup> More recently, the terpenoids of lemon balm have been shown to inhibit HSV-2 replication.<sup>10</sup>

In another double-blind clinical trial, a cream formula that combined aqueous extracts of the mint family plant *Salvia officinalis* (sage) leaf with *Rheum palmatum* (Chinese rhubarb) root was just as effective as acyclovir cream and significantly more effective than sage cream by itself at healing herpes labialis.<sup>11</sup> Average time to complete healing with the combined cream was 6.7 days, compared to 6.5 days for acyclovir. No significant adverse effects were reported. The trial was fairly large (total 145 immunocompetent participants), making the results fairly strong. The mechanisms of action of sage have not been clarified though this herb is definitely antioxidant and has a long history of use for treating infections of all sorts.<sup>12</sup> An early study was reported to have found that rhubarb cream alone was ineffective.<sup>13</sup>

No other clinical trials of mint family plants were identified. Other potentially useful herbs in this category to consider are *Prunella vulgaris* (heal all) aerial parts, *Thymus serpyllum* (wild thyme) leaf, *Nepeta cataria* (catnip) leaf, *Origanum vulgare* (oregano) leaf, and *Mentha* spp. (mint) leaf. In one study of traditional

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## Clinical Review of Herpes Simplex

### Types of herpes viruses

*HSV-1*—primarily infects patients by direct contact with saliva above the waist, but can cause genital infections. The virus goes dormant in sensory ganglion cells of trigeminal ganglia in the brainstem. An infection can be reactivated by stress (physical or mental), immune suppression, menses and other hormonal shifts, and/or environmental fluctuations.

*HSV-2*—infects patients by direct sexual contact below the waist, but can cause oral lesions. Transmission of both types can occur when there are no visible lesions present. Goes dormant in sacral or lumbar ganglia. Reactivation similar to HSV-1.

### Signs and symptoms

Herpes labialis or genitalis can manifest with a prodromal tingle or itch for 1–2 days followed by crops of painful, fluid-filled vesicles on erythematous bases. The vesicles burst after 5–7 days creating yellow-crust lesions that heal 12–21 days after the outbreak begins without treatment. Scarring may occur if outbreaks affect the same area repeatedly.

Initial infection may cause more severe symptoms and fever and systemic myalgia.

The virus can also cause ophthalmitis or central nervous system (CNS) disease in neonates or immunosuppressed people.

### Diagnosis

Diagnosis is made generally by clinical examination but can be confirmed by rising viral titers, Tzanck smear, or viral culture when presentation is unusual.

Mexican HSV remedies, *Mentha piperata* (mint) and *Ocimum basilicum* Lineo (basil) displayed the strongest activity in vitro.<sup>14</sup> A study of aqueous extracts of a number of mints (lemon balm, peppermint, heal all, rosemary, sage, and thyme) all showed strong antiviral activity against HSV-1 in vitro. This study concluded that the mints exert their effect on HSV before adsorption and should work well topically.<sup>15</sup> Another study of basil fractions found that its ursolic acid had the strongest activity against HSV-1 in vitro.<sup>16</sup> We often combine lemon balm with another mint-family plant in our antiherpes topical formulas.

Heal all has a long history of use for viral infections and its anti-HSV mechanisms have been studied more closely than those of other mints. In guinea pigs, a cream made from a semi-purified fraction (lignin–polysaccharide complex) from heal all significantly reduced skin lesions and inhibited viral binding and penetration into host cells.<sup>17</sup> Heal all inhibits HSV by a different mechanism than acyclovir, potentially via suppression of antigen expression.<sup>18</sup> Polysaccharides seem critical to the antiherpetic efficacy of this herb and have also been shown to block HSV entry into cells, possibly through receptor blockade.<sup>19</sup> However, other constituents in mints may be equally important to their activity.

## The Role of Tannins

Tannins come in two forms, condensed and hydrolyzable. Condensed tannins are large flavonoid polymers, whereas hydrolyzable tannins have a glucose core with attached gallic

or ellagic acid units. Older studies focused on the tannins in mints as important antiviral constituents.<sup>20,21</sup>

More-recent laboratory studies have found that simple hydrolyzable tannins are potent antiherpetic agents and act by blocking viral adsorption to human cells.<sup>22</sup> Many tannin-rich herbs have been shown to inhibit HSV in vitro. For instance, *Punica granatum* (pomegranate) pericarp blocked HSV replication as well as adsorption.<sup>23</sup> *Geranium sanguineum* (bloody cranesbill) aqueous root extract, rich in tannins, blocked HSV replication and cytopathogenicity in vitro and delayed vesiculation when administered orally to guinea pigs after primary infection.<sup>24</sup> A close relative of this herb is frequently used in the West, *Geranium maculatum* (cranesbill), in a similar fashion. *Crataegus sinaica* (Chinese hawthorn) contains proanthocyanidins, flavonoid oligomers that are precursors to condensed tannins, and was shown to inhibit HSV activity in vitro.<sup>25</sup> Other species of hawthorn (*C. aronia*, *C. monogyna*, and *C. pseudoheterophylla*) also have shown strong HSV inhibitory activity in vitro.<sup>26</sup> There are others but these suggest that tannins have relevant anti-HSV activity.

One clinical trial investigating a method of assessing efficacy of antiherpes drugs studied a topical combination of isolated tannic acid and salicylic acid.<sup>27</sup> The authors found that the study medication greatly speeded reduction in size of lesions compared to baseline, whereas placebo was much weaker in this regard. Although this proof-of-concept study was small and did not use true between-group comparisons, it does give some initial sense that tannins can be therapeutically useful when applied topically.

In clinical practice, it is observed that tannin-rich herbs are particularly useful topically when vesicles are starting to burst and weep. The tannins adsorb proteins in the exudates and help relieve symptoms. We often include tannin-rich herbs in topical formulas for these effects as well as their antiviral effects.

## Intriguing Antivirals from China

Numerous other herbs have shown potential as antiherpes treatments. As mentioned above, Chinese rhubarb root is one of these that has been shown to be effective, combined with sage, for treating patients with herpes labialis. Though Chinese rhubarb contains tannins that might explain its activity, most research has focused on the anthraquinones in this plant, which are most renowned for their cathartic laxative properties in higher doses. One study found that anthraquinones from Chinese rhubarb as well as several other herbs, including *Frangula purshiana* (cascara sagrada) bark, *Rhamnus frangula* (alder buckthorn) root, *Senna alexandrina* (cassia) leaf, and *Aloe barbadensis* latex, were virucidal to HSV and other enveloped viruses in vitro.<sup>28</sup> Injection of an ethanolic extract of Chinese rhubarb, presumably low in tannins (as the compounds are quite toxic when present in high concentrations in the body), in mice infected with HSV, was as effective as acyclovir in one

Chinese study.<sup>29</sup> Ethanol extract of Chinese rhubarb blocked HSV attachment and penetration in vitro.<sup>30</sup>

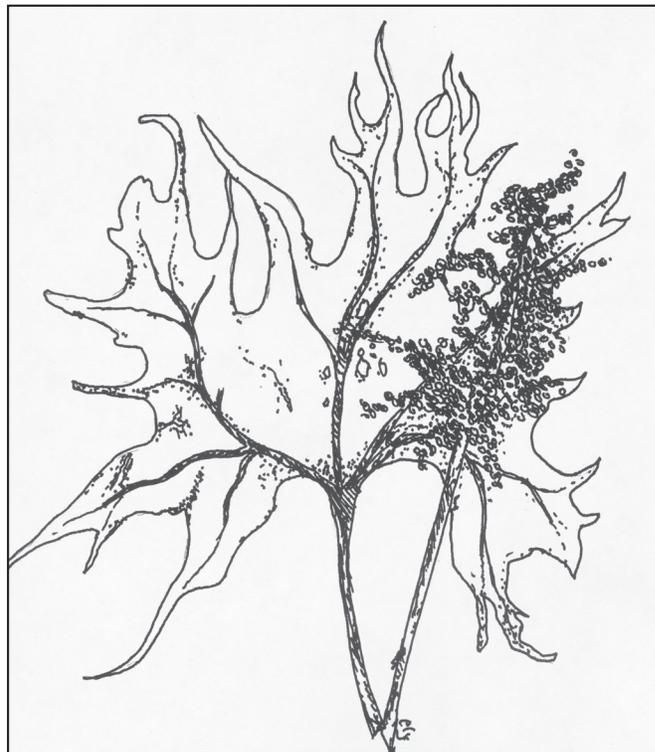
*Melia azedarach* (China tree, chinaberry) root bark and fruit are traditional Chinese remedies for many infectious diseases. A limonoid compound from the leaves of this tree was shown to inhibit HSV in vitro.<sup>31</sup> A protein from the leaves, meliacine, has been more extensively studied and shown to interfere with HSV DNA synthesis and viral maturation and envelope formation.<sup>32</sup> This protein inhibited formation of herpetic keratitis in a mouse study when applied topically, whereas placebo had no protective effect.<sup>33</sup> A compound in the fruit, 28-deacetylsendanin, has been shown to block HSV replication and to reduce HSV thymidine kinase production.<sup>34</sup> Another study concluded that chinaberry compounds not only inhibit replication but also act as immunomodulators.<sup>35</sup> We believe whole-herb extracts of this plant need to be studied to find out if synergy among the various constituents provide equally or more-effective results. At least one study of an aqueous extract of a close relative, *Melia toosendan*, has shown that it can prevent viral attachment in vitro.<sup>30</sup>

### Other Antiherpetic Herbs

The volatile oil of *Melaleuca alternifolia* (tea tree) leaf is popular as an antifungal. However, in vitro, it is also a potent blocker of HSV adsorption.<sup>36</sup> Tepinen-4-ol was found to be a stronger antiherpetic than total volatile oil of tea tree, apparently because other terpenoids in the mixture were reducing its water solubility significantly.<sup>37</sup> A preliminary, single-blind clinical trial of a gel product containing 6% tea tree volatile oil in immunocompetent patients with recurrent herpes labialis found some improvement with the gel but statistical significance compared to placebo was not achieved.<sup>38</sup> This is not surprising given the very small sample size of the study ( $n = 20$ ). Further study of tea tree and other antiviral volatile oils is warranted to determine their efficacy.

Propolis is a mixture of compounds harvested by bees from the resin of various trees, most notably members of the Salicaceae (willow) family. Propolis mixtures have been shown more active against HSV in vitro than single propolis flavonoids.<sup>39</sup> A minor caffeic-acid derivative in propolis has been shown to inhibit HSV DNA synthesis in vitro.<sup>40</sup> In a single-blind clinical trial, topical application of 3% propolis ointment was found to be significantly more effective than acyclovir or placebo at resolving lesions and symptoms of genital herpes in men and women.<sup>41</sup> Unlike acyclovir or placebo, the propolis ointment was also effective at treating vaginal superinfections in those women with intravaginal or cervical herpetic lesions. These promising results should be confirmed in larger clinical trials.

*Hypericum perforatum* (St. John's wort) is a traditional treatment for herpes and other viral infections. A number of in vitro studies have found that various species in the *Hypericum* genus inhibit HSV, though one study conclud-



*Rheum palmatum* (Chinese rhubarb). Drawing ©Eric Yarnell, N.D.

ed this activity was much weaker than the other two.<sup>42–45</sup> Different extracts, concentrations, cell models, and timings of application could easily explain the variability of these preclinical studies. St. John's wort has also shown wound-healing activity that makes the herb particularly suitable for topical administration.<sup>46</sup>

The final group of antiviral herbs we mention are various algae (seaweeds) that contain sulfated polysaccharides such as *Prionitis lyallii* (red dulse). It is believed that these compounds act by blocking viral adsorption to cells. For a list of selected studies on various red algae and seaweeds that have been shown to have antiherpetic effects, see Table 1. We have encountered many patients with excellent results both from topical and oral preparations of various red-algae products. Unfortunately, no clinical trials were located but are urgently needed.

It should be emphasized that, although most recent HSV studies investigate topical preparations or the antiviral activities of plants in vitro, most practitioners use plants both internally and topically in HSV. Although there are some studies indicating the benefit of orally administered herbs to prevent or mitigate HSV eruptions, most of these studies are in relatively obscure foreign journals and their abstracts provide little information. Reportedly, an orally administered St. John's wort extract (LI 160) showed some benefit in two placebo-controlled, double-blind studies.<sup>47</sup> It was also reported that an infusion of various Japanese herbs was an "effective treatment for herpes genitalis and herpes labialis."<sup>48</sup> In addition, studies indicate that a number of herbs and botanicals arrested or delayed the formation of vesicles and prolonged



*Echinacea* spp. (echinacea).

survival times when administered to animals coinfectd with HSV and HIV.<sup>49–52</sup>

We have frequently used herbs internally with some success, often in formulas that include both lemon balm and St. John's wort. If a patient notices the onset of an acute outbreak and begins taking a combination of antivirals right away, he or she can sometimes abort the attack entirely. Other patients have significantly extended the time between attacks or had much milder attacks by using a formula that includes both antiviral and adaptogenic herbs (see below).

Finally, another area ripe for further research is the use of herbs as synergists to pharmaceutical antivirals or as a treatment in drug-resistant HSV infections. There are preliminary studies that indicate that several herbs potentiated the action of acyclovir in in vitro and in vivo studies.<sup>53</sup>

## Immune Therapies for Herpes

A complete, holistic treatment of a patient with HSV requires the use of herbs that directly interfere with HSV and herbs that support the immune system. This is particularly important in patients who are immunosuppressed due to chemotherapy or HIV infection. Of course, patients who are on immunosuppressive drugs must be approached much more cautiously as immunomodulating herbs may interfere with these drugs and cause organ rejection.

In this context, we suggest herbs that have a tonic (or long-term) immune-building effect rather than herbs that are typically used for acute issues. *Echinacea* spp. is an example of the latter. Besides being a macrophage stimulator, various extracts of various species have been shown to be anti-HSV in vitro, with the presence of alkenes and alkylamides being most associated with inhibition.<sup>54</sup> A clinical trial compared the leaf and flower juice of *Echinacea purpurea*, which is relatively low in alkylamides compared to the root of *E. angustifolia* or *E. pallida*, with placebo in a double-blind, crossover trial.<sup>55</sup> Over 1 year's time, there was no difference in the number or severity of infections found between the groups.

In contrast are herbs that have a broader effect on the immune system mediated by their effects on CD4+ T helper lymphocytes, such as *Astragalus membranaceus* root. In a clinical trial conducted in China, patients with herpetic keratitis were treated with either astragalus or ribavirin with uncertain blinding conditions.<sup>56</sup> Subjects who received astragalus had a definite improvement in immune parameters not seen during ribavirin treatment. Results on actual progression of the infection were not reported, as the full text of this Chinese-language study was not available for complete assessment. A topical formulation of astragalus combined with interferon has been shown to be more effective than interferon alone at inhibiting HSV in vitro.<sup>57</sup> At fairly high concentrations, astragalus is directly anti-HSV in vitro.<sup>58</sup> Taken

**Table 1. Selected Antiherpetic Seaweeds**

Name	Origin	Research
<i>Pterocladia capillacea</i>	Uruguay	Blocks HSV adsorption in vitro*
<i>Gymnogongrus griffithsiae</i> and <i>Cyrtoneimia crenulata</i>	Brazil	Blocks HSV adsorption in vitro and in murine vaginal model†
<i>Nothogenia fastigiata</i>	Argentina	Blocks HSV adsorption in vitro‡
<i>Bostrychia montagnei</i>	South American coast	Blocks HSV adsorption in vitro, no effect on blood clotting§
<i>Gracilaria corticata</i>	India	Inhibits HSV adsorption

HSV, herpes simplex virus.

References: \*Pujol CA, Errea MI, Matulewicz MC, et al. Antiherpetic activity of S1, an algal-derived sulphated galactan. *Phytother Res* 1996;10:410–413.

†Talarico LB, Zibetti RG, Faria PC, et al. Antiherpes simplex virus activity of sulfated galactans from the red seaweeds *Gymnogongrus griffithsiae* and *Cyrtoneimia crenulata*. *Int J Biol Macromol* 2004;34:63–71.

‡Damonte EB, Matulewicz MC, Cerezo AS, et al. Herpes simplex virus-inhibitory sulfated xylogalactans from the red seaweed *Nothogenia fastigiata*. *Chemotherapy* 1996;42:57–64.

§Duarte ME, Nosedá DG, Nosedá MD, et al. Inhibitory effect of sulfated galactans from the marine alga *Bostrychia montagnei* on herpes simplex virus replication in vitro. *Phyto-medicine* 2001;8:53–58.

||Mazumder S, Ghosal PK, Pujol CA, et al. Isolation, chemical investigation and antiviral activity of polysaccharides from *Gracilaria corticata* (Gracilariaceae, Rhodophyta). *Int J Biol Macromol* 2002;31:87–95.

together, these studies suggest that more work should be done to determine whether astragalus would be a good immune tonic for preventing or treating herpes infections.

Adaptogens are herbs that are used to strengthen individuals contending with chronic conditions. They include plants such as *Eleutherococcus senticosus* (eleuthero) root, *Rhodiola rosea* (goldenroot) root, medicinal mushrooms, *Schisandra chinensis* (wu wei) fruit, and others. We highly recommend the inclusion of individually chosen adaptogenic herbs to lessen the severity and frequency of outbreaks in patients with HSV.

## Clinical Application

Several herbal medicines have been shown to be effective and safe for treatment of patients with herpes simplex in clinical trials, most notably lemon balm, sage, Chinese rhubarb, propolis, and tea tree. These antiviral herbs, or ones similar to them, form an important basis for natural regimens for patients with herpes. Tannin-rich herbs are also frequently used topically to help relieve symptoms, and have many documented anti-HSV effects. We have also had many good results using several antiherpetic herbs internally as well as topically, though this has not yet been the subject of rigorous clinical trials.

We have generally found that creams are acceptable and can be effective for relieving herpes outbreaks, but that topical application of tinctures can be even more immediately helpful. This is because ethanol has a drying effect that quickly reduces pain. Unfortunately, this is not as cosmetically acceptable and may even stain the skin for several hours' time, and thus most patients opt to apply tincture in the evening when not at work and to use cream throughout the day. It cannot be sufficiently stressed that multiple applications of any topical herbal compounds are necessary for full efficacy, and that they should be started as soon as prodromal symptoms are noted or lesions appear, whichever comes first. Oils and ointments are not as effective and may actually spread the lesions.

Added to topical antivirals are various adaptogenic, immunomodulating herbs that potentiate the patient's own ability to fight the virus. While not as well-documented to be effective, we have consistently found them to be helpful. They are particularly vital in immunosuppressed patients, but should not be combined with immunosuppressive drugs.

We have found that a full herbal protocol coupled with nutritional recommendations and stress reduction can cost-effectively and safely help most patients with herpes infections. ■

## References

- Schillinger JA, Xu F, Sternberg MR, et al. National seroprevalence and trends in herpes simplex virus type 1 in the United States, 1976–1994. *Sex Transm Dis* 2004;31:753–770.
- Celum C, Levine R, Weaver M, et al. Genital herpes and human immunodeficiency virus: Double trouble. *Bull World Health Organ* 2004;82:447–453.
- Kimberlin DW, Whitley RJ. Neonatal herpes: What have we learned. *Semin Pediatr Infect Dis* 2005;16:7–16.

- Stranska R, Schuurman R, Nienhuis E, et al. Survey of acyclovir-resistant herpes simplex virus in the Netherlands: Prevalence and characterization. *J Clin Virol* 2005;32:7–18.
- Wölbling RH, Milbradt R. Clinical and therapeutic approaches to herpes simplex: Introduction of a new phytotherapeutic active substance [in German]. *Therapiewoche* 1984;34:1193–1200.
- Wölbling RH, Leonhardt K. Local therapy of herpes simplex with dried extract of *Melissa officinalis*. *Phytomedicine* 1994;1:25–31.
- Koytchev R, Alken RG, Dundarov S. Balm mint extract (Lo-701) for topical treatment of recurring herpes labialis. *Phytomedicine* 1999;6:225–230.
- Vogt M, Tausch I, Wolbling RH, et al. *Melissa* extract in herpes simplex: A double-blind placebo-controlled study [in German]. *Der Allgemeinarzt* 1991;13:832–841.
- Dimitrova Z, Dimov B, Manolova N, et al. Antiherpes effect of *Melissa officinalis* L. extracts. *Acta Microbiol Bulg* 1993;29:65–72.
- Allahverdiyev A, Duran N, Ozguven M, et al. Antiviral activity of the volatile oils of *Melissa officinalis* L. against herpes simplex virus type-2. *Phyto-medicine* 2004;11(7–8):657–661.
- Saller R, Buechi S, Meyrat R, et al. Combined herbal preparation for topical treatment of herpes labialis. *Forsch Komplementarmed Klass Naturheilkd* 2001;8:373–382.
- Hohmann J, Zupko I, Redei D, et al. Protective effects of the aerial parts of *Salvia officinalis*, *Melissa officinalis* and *Lavandula angustifolia* and their constituents against enzyme-dependent and enzyme-independent lipid peroxidation. *Planta Med* 1999;65:576–578.
- Buechi S. Sage leaves and rhubarb roots versus aciclovir [sic] in treating herpes labialis [in German]. *Zeitschrift Phytother* 2005;26:275–277.
- Ramirez MME, Vazquez CS, Barron RBL. Antiviral effect of three vegetal infusions (*Mentha piperata*, *Cinnamomum zeylanicum* Blume and *Ocimum basilicum* Lineo) on a murine herpetic infection. *Revista Mex de Ciencias Farmaceut* 1998; 29:17–24.
- Nolkemper S, Reichling J, Stintzing FC, et al. Antiviral effect of aqueous extracts from species of the Lamiaceae family against herpes simplex virus type 1 and type 2 in vitro. *Planta Med* 2006;72:1378–1382.
- Chiang L-C, Ng L-T, Cheng P-W, et al. Antiviral activities of extracts and selected pure constituents of *Ocimum basilicum*. *Clin Exp Pharmacol Physiol* 2005;32:811–816.
- Zhang Y, But PP-H, Ooi VE-C, et al. Chemical properties, mode of action, and in vivo antiherpes activities of a lignin-carbohydrate complex from *Prunella vulgaris*. *Antiviral Res* 2007;75:242–249.
- Chiu LC, Zhu W, Ooi VE. A polysaccharide fraction from medicinal herb *Prunella vulgaris* down regulates the expression of herpes simplex virus antigen in Vero cells. *J Ethnopharmacol* 2004;93:63–68.
- Xu HX, Lee SH, Lee SF, et al. Isolation and characterization of an anti-HSV polysaccharide from *Prunella vulgaris*. *Antiviral Res* 1999;44:43–54.
- Kucera LS, Herrmann EC Jr. Antiviral substances in plants of the mint family (Labiatae): I. Tannin of *Melissa officinalis*. *Proc Soc Exp Biol Med* 1967;124:865–869.
- Herrmann EC Jr, Kucera LS. Antiviral substances in plants of the mint family (Labiatae): 3. Peppermint (*Mentha piperita*) and other mint plants. *Proc Soc Exp Biol Med* 1967;124:874–878.
- Fukuchi K, Sakagami H, Okuda T, et al. Inhibition of herpes simplex virus infection by tannins and related compounds. *Antiviral Res* 1989;11:285–297.
- Zhang J, Zhan B, Yao X, et al. Antiviral activity of tannin from the pericarp of *Punica granatum* L. against genital herpes virus in vitro [in Chinese]. *Zhongguo Zhong Yao Za Zhi* 1995;20:556–558,576, inside back cover.
- Serkedjjeva J, Ivancheva S. Antiherpes virus activity of extracts from the medicinal plant *Geranium sanguineum* L. *J Ethnopharmacol* 1999;64:59–68.
- Shahat AA, Cos P, De Bruyne T, et al. Antiviral and antioxidant activity of flavonoids and proanthocyanidins from *Crataegus sinaica*. *Planta Med* 2002;68:539–541.

26. Orhan I, Ozcelik B, Kartal M, et al. HPLC quantification of vitexine-2'-O-rhamnoside and hyperoside in three *Crataegus* species and their antimicrobial and antiviral activities. *Chromatographia* 2007;66(suppl):S53–S157.
27. Rodu B, Russell CM, Mattingly G. Determining therapeutic efficacy in recurrent herpes labialis by lesion-size analysis. *Oral Surg Oral Med Oral Pathol* 1991;72:178–183.
28. Sydiskis RJ, Owen DG, Lohr JL, et al. Inactivation of enveloped viruses by anthraquinones extracted from plants. *Antimicrob Agents Chemother* 1991;35:2463–2466.
29. Wang ZY, Xu B, Song YY, et al. Inhibition effects of rhubarb ethanol extract on herpes simplex virus infection in vivo [in Chinese]. *Zhonghua Shi Yan He Lin Chuang Bing Du Xue Za Zhi*. 2003;17:169–173.
30. Hsiang CY, Hsieh CL, Wu SL, et al. Inhibitory effect of anti-pyretic and anti-inflammatory herbs on herpes simplex virus replication. *Am J Chin Med* 2001;29:459–467.
31. Alche LE, Ferek GA, Meo M, et al. An antiviral meliicarpin from leaves of *Melia azedarach* L. *Z Naturforsch [C]* 2003;58:215–219.
32. Alche LE, Barquero AA, Sanjuan NA, et al. An antiviral principle present in a purified fraction from *Melia azedarach* L. leaf aqueous extract restrains herpes simplex virus type 1 propagation. *Phytother Res* 2002;16:348–352.
33. Pifarre MP, Berra A, Coto CE, et al. Therapeutic action of meliacine, a plant-derived antiviral, on HSV-induced ocular disease in mice. *Exp Eye Res* 2002;75:327–334.
34. Kim M, Kim SK, Park BN, et al. Antiviral effects of 28-deacetylsendanin on herpes simplex virus-1 replication. *Antiviral Res* 1999;43:103–112.
35. Barquero AA, Michelini FM, Alche LE. 1-cinnamoyl-3,11-dihydroxymeliicarpin is a natural bioactive compound with antiviral and nuclear factor-kappaB modulating properties. *Biochem Biophys Res Comm* 2006;344:955–962.
36. Schnitzler P, Schon K, Reichling J. Antiviral activity of Australian tea tree oil and eucalyptus oil against herpes simplex virus in cell culture. *Pharmazie* 2001;56:343–347.
37. Cox SD, Mann CM, Markham JL. Interactions between components of the essential oil of *Melaleuca alternifolia*. *J Appl Microbiol* 2001;91:492–497.
38. Carson CF, Ashton L, Dry L, et al. *Melaleuca alternifolia* (tea tree) oil gel (6%) for the treatment of recurrent herpes labialis. *J Antimicrob Chemother* 2001;48:450–451.
39. Amoros M, Simoes CM, Girre L, et al. Synergistic effect of flavones and flavonols against herpes simplex virus type 1 in cell culture: Comparison with the antiviral activity of propolis. *J Nat Prod* 1992;55:1732–1740.
40. Amoros M, Lurton E, Boustie J, et al. Comparison of the antiherpes simplex virus activities of propolis and 3-methyl-but-2-enyl caffeate. *J Nat Prod* 1994;57:644–647.
41. Vynograd N, Vynograd I, Sosnowski Z. A comparative multicentre study of the efficacy of propolis, acyclovir, and placebo in the treatment of genital herpes (HSV). *Phytomedicine* 2000;7:1–6.
42. Vijayan P, Raghu C, Ashok G, et al. Antiviral activity of medicinal plants of Nilgiris. *Indian J Med Res* 2004;120:24–29.
43. Sokmen A, Jones BM, Erturk M. Antimicrobial activity of extracts from the cell cultures of some Turkish medicinal plants. *Phytother Res* 1999;13:355–357.
44. Taylor RS, Manandhar NP, Hudson JB, et al. Antiviral activities of Nepalese medicinal plants. *J Ethnopharmacol* 1996;52:157–163.
45. Fritz D, Venturi CR, Cargin S, et al. Herpes virus inhibitory substances from *Hypericum connatum* Lam., a plant used in Southern Brazil to treat oral lesions. *J Ethnopharmacol* 2007;113:517–520.
46. Mukherjee PK, Suresh B. The evaluation of the wound-healing potential of *Hypericum hookerianum* leaf and stem extracts. *J Altern Complement Med* 2000;6:61–69.
47. Koytchev R, Alken RG, Dundarov S. *Hypericum* extract LI 160 for the therapy of herpes simplex genitalis and labialis: Results of two placebo-controlled, randomized, double-blind clinical trials [in German]. *Z Phytother* 1999;20:92.
48. Hijikata Y, Tsukamoto Y. Effect of herbal therapy on herpes labialis and herpes genitalis. *Biother* 1998;11:235–240.
49. Kurokawa M, Nakando M, Ohyama H, et al. Prophylactic efficacy of traditional herbal medicines against recurrent herpes simplex virus type 1 infection from latently infected ganglia in mice. *J Dermatol Sci* 1997;14:76–84.
50. Nawawi A, Nakamura N, Meselhy MR, et al. In vivo antiviral activity of *Stephania cepharantha* against herpes simplex virus type-1. *Phytother Res* 2001;15:497–500.
51. Kurokawa M, Ochiai H, Nagasaka K, et al. Antiviral traditional medicines against herpes simplex virus (HSV-1), poliovirus, and measles virus in vitro and their therapeutic efficacies for HSV-1 infection in mice. *Antiviral Res* 1993;22:175–188.
52. Serkedjieva J, Ivancheva S. Antiherpes virus activity of extracts from the medicinal plant *Geranium sanguineum* L. *J Ethnopharmacol* 1999;64:59–68.
53. Kurokawa M, Nagasaka K, Hirabayashi T, et al. Efficacy of traditional herbal medicines in combination with acyclovir against herpes simplex virus type 1 infection in vitro and in vivo. *Antiviral Res* 1995;27:19–37.
54. Binns SE, Hudson J, Merali S, et al. Antiviral activity of characterized extracts from *Echinacea* spp. (Heliantheae: Asteraceae) against herpes simplex virus (HSV-1). *Planta Med* 2002;68:780–783.
55. Vonau B, Chard S, Mandalia S, et al. Does the extract of the plant *Echinacea purpurea* influence the clinical course of recurrent genital herpes? *Int J STD AIDS* 2001;12:154–158.
56. Mao SP, Cheng KL, Zhou YF. Modulatory effect of *Astragalus membranaceus* on Th1/Th2 cytokine in patients with herpes simplex keratitis [in Chinese]. *Zhongguo Zhong Xi Yi Jie He Za Zhi* 2004;24:121–123.
57. Zhang L, Liu Y, Yu Z. Study on the anti-herpes simplex virus activity of a suppository or ointment form of *Astragalus membranaceus* combined with interferon alpha 2b in human diploid cell culture [in Chinese]. *Zhonghua Shi Yan He Lin Chuang Bing Du Xue Za Zhi* 1998;12:269–271.
58. Sun Y, Yang J. Experimental study of the effect of *Astragalus membranaceus* against herpes simplex virus type 1 [in Chinese]. *Di Yi Jun Yi Da Xue Xue Bao* 2004;24:57–58.

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