Promising Herbs and Phytochemicals for Chronic Hepatitis C Virus Infection

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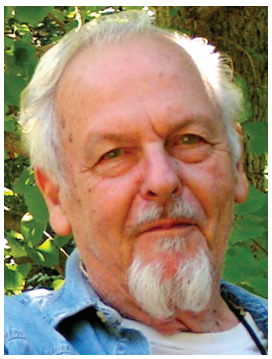

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According to Thorn and Associates (1999), "Hepatitis C virus (HCV) is the most common chronic blood-borne infection in the United States. An estimated 3.9 million Americans (1.4%) are infected with HCV. The 10th leading cause of death in U.S. adults is chronic liver disease (CLD), which accounts for 25,000 deaths annually. Approximately 40% of all CLD is related to HCV, causing 8000 to 10,000 deaths annually. In addition, approximately 60% of people with HIV are believed to be co-infected with HCV, which hastens their progression to AIDS" (PMID 11094970). Even today, Bastos et al. (2016) says, "Despite advances in therapy, hepatitis C virus (HCV) infection remains an important global health issue. It is estimated that a significant part of the world population is chronically infected with the virus, and many of those affected may develop cirrhosis or liver cancer. The virus shows considerable variability, a characteristic that directly interferes with disease treatment. The response to treatment varies according to HCV genotype and subtype...Researchers should consider the mutation capacity of the virus and the other variables that affect treatment success" (PMID 27605875). [Editor's note: PMID numbers reference articles in the database PubMed at http://www.ncbi.nlm.nih.gov/pubmed.]

Small wonder that there are many reported herbal antivirals, as researchers grasp for straws

Glycyrrhiza glabra (licorice) inflorescence – the root is used medicinally

(or grasp for reality?) in the face of this monster. I searched my database for antihepatitis (antihepatotic) herbs and spices and there were nearly a hundred species. Records from the Evibase (Duke 2014b) are scored for level of evidence: "f" being folk or traditional evidence, "1" being lower level scientific evidence, "2" being epidemiological or chemical evidence, and "3" being clinical evidence. Several of the species attained a score of "2" or above, including *Pimpenella anisum* (anise), *Cynara cardunculus* (artichoke), *Scutellaria baicalensis* (Baikal skullcap), *Peumus boldo* (boldo), *Carum carvi* (caraway), *Elettaria cardamomum* (cardamom), *Matricaria chamomilla* (chamomile), *Cichorium intybus* (chicory), *Mentha arvensis* (field mint), *Andrographis paniculata* (creat), *Anethum graveolens* (dill), *Angelica sinensis* (dong quai), *Alpinia officinarum* (lesser galangal), *Marrubium vulgare* (horehound), *Hyssopus officinalis* (hyssop), *Orthosiphon stamineus* (Java tea), *Glycyrrhiza glabra* (licorice), *Schisandra chinensis* (schisandra), *Silybum marianum* (milk thistle), *Mentha x piperita* (peppermint), *Rosmarinus officinalis* (rosemary), *Santalum* spp. (sandalwood), *Curcuma longa* (turmeric), and *Artemisia absinthium* (wormwood). Anything scoring a "2" in my system should be clinically compared with competitive synthetic pharmaceutical antivirals before we dismiss such herbs as useless. (As a confirmation of completeness, my database has most of the first 250 and last 250 entries for herbs for hepatitis in PubMed.)

In his useful and insightful book *Herbs for Hepatitis C and the Liver,* Stephen Harrod Buhner (2000) lists his "Top 10 Botanical Medicines for Hepatitis C" as: Baikal skullcap, boldo, *Bupleurum* spp., *Arctium lappa* (burdock), *Taraxacum officinale* (dandelion), milk thistle, *Phyllanthus* spp. (leafflower), *Picrorhiza kurroa* (kutki), *Ganoderma* spp. (reishi mushroom), and turmeric; and his "10 Major Immune Tonic Herbs for Hepatitis" as *Withania somnifera* (ashwagandha), *Astragalus membranaceus* (huang qi), *Eupatorium perfoliatum* (boneset), *Codonopsis pilosula* (dang shen), licorice, *Panax ginseng* (Asian ginseng), *Ceanothus* spp. (red root), schisandra, *Eleutherococcus senticosus* (Siberian ginseng), and *Panax notoginseng* (Tienchi ginseng).

Between Buhner's top ten lists and the top antihepatotic herbs scoring "2" in my system, there are eight species that I believe could be the most promising: Baikal skullcap, boldo, licorice, schisandra, milk thistle, Asian ginseng, leafflower, and reishi mushroom. These are all good and reasonably safe herbs, and many are aliens or introduced in the Americas, so readily available and not classified as threatened or endangered. Buhner adds that herbal clinicians and scientists researching

Picrorhiza kurroa (kutki) is listed in Appendix II of the Convention on International Trade in Endangered Species (CITES) due to overharvesting in the wild

Suresh Rana, Flowers of India, CC BY-SA 2.0

Phyllanthus niruri (stonebreaker, seed-under-leaf) is one common member of the *Phyllanthus* (leafflower) genus

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… herbs can be as good as pharmaceuticals and better at reaching body areas that pharmaceutical cannot reach…We need a controlled and honest clinical comparison.

HCV (in vitro, in vivo, and in human trials) say that the herbs display exceptional strength: "In a majority of patients, symptoms resolve, liver enzyme levels normalize, and viral loads often disappear." Citing Matthew Dolan's *The Hepatitis C Handbook*, Buhner (2000) says that Austrian research suggests that herbs can be as good as pharmaceuticals and better at reaching body areas that pharmaceutical cannot reach.

Probably the most widely used pharmaceuticals for HCV (and often used together) are pegylated interferon (an immune stimulant) and ribavirin (an antiviral). Buhner notes that the most common side effect (for about 80% of patients) "is similar to a moderate case of the flu – for the whole year of treatment… The primary side effect of ribavirin is hemolysis" (rupturing of red blood cells). Buhner suggests that interferon alone is effective in only about 15% of patients. Many researchers doubt that ribavirin has an antiviral effect at all. Interferon and ribavirin together may synergistically succeed in 35% of cases. But most of the world cannot afford the $10,000 a year it costs. The poor of the world may fare better on herbs than the wealthy on pharmaceuticals. We need a controlled and honest clinical comparison.

Ceanothus americanus (New Jersey tea, red root) – the root is used medicinally

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Another attractive target for drug design and development is the NS3-4A serine protease, where inhibitors may reduce expression of NS3, which is important for the HCV life cycle (PMID12505640). A number of antivirals against HCV infection are in clinical progress, including NS3-4A protease inhibitors, RNA-dependent RNA polymerase inhibitors, and NS5A inhibitors, as well as host targeted inhibitors. Two NS3-4A protease inhibitors (telaprevir and boceprevir) have been recently approved for the treatment of hepatitis C in combination with the standard interferon-plus-ribavirin treatment. The new therapy has significantly improved the virologic response, however, the adverse effects associated with this new therapy (i.e., severe anemia, impairment of CYP450-3A4 liver detoxification pathways leading to drug-drug interactions) bring their value into question (Salam and Akimitsu 2013). Our database fortunately shows a number of herbs and spices that have NS3 protease inhibitory actions.

In addition to causing chronic hepatitis, the worldwide scourge of HCV infection may also lead to liver cirrhosis and the primary liver cancer, Hepatocellular carcinoma (HCC). HCC is frequent in patients with chronic hepatitis and cirrhosis caused by persistent HCV. More so than HCV, Hepatitis B infection (HBV) may lead to liver cancer and other liver diseases. The risk of HCC increases with progression of the hepatic fibrosis associated with chronic hepatitis and liver cirrhosis. Hence, antifibrotics may help to decrease the risk of HCC. It has been shown that some antifibrotic agents (e.g., prolyl 4-hydroxylase inhibitor [HOE 077], Kampo herbal compound sho-saiko-to [TJ-9], interferon) can reduce risk of

Ganoderma lucidum (ling zhi, reishi) mushroom

HCC (PMID11868781). Other suspected liver cancer causes include abuse of alcohol, *Piper betle* (betel), and *Nicotiana tabacum* (tobacco) (PMID1645698; PMID1655259; PMID12632815). I have included antifibrotic agents in the search of our databases for herbal help in fighting HCV.

Generous use of hepatoprotective herbs and spices as greens, soups, teas, and vegetables can slow a gradually progressive HCV infection. The healing foods movement might also embrace real or marginal food crops like *Achillea millefolium* (yarrow), burdock root (gobo), *Camellia sinensis* (green tea), chicory, artichoke, *Morinda citrifolia* (noni), *Rheum* spp. (rhubarb), and dandelion. My databases can tell which edible herbs and phytochemicals have the best specific evidence for immunostimulant, antihepatotic, antifibrotic, NS3 protease inhibitor, or antiHCV actions, as detailed in Table 1.

Table 1. AntiHCV and Antihepatotic Herbs

Species	Common Name	Activity Categories	Citation(s)
Acacia confusa	small acacia	AntiHCV via NF-kappaB inhibitor	PMID21075144
Acacia nilotica	gum Arabic tree methanol extract	AntiHCV; HCV protease inhibitor via *IC90=100ug/ml	PMID21569385, PMID11054840
Achillea millefolium	yarrow	AntiHCV	Duke 2014b, PMID18271298
Alpinia galanga	greater galangal	AntiHCV; HCV protease inhibitor	PMID16964717
Alpinia officinarum	lesser galangal	AntiHCV	Duke 2014b
Amelanchier alnifolia	serviceberry	AntiHCV via Quercitin-3-galactoside; HCV NS3-4A helicase inhibitor; HCV NS3-4A protease inhibitor	PMID24391361
Andrographis paniculata	creat, chiretta	Antihepatotic	Duke 2014b
Anethum graveolens	dill	AntiHCV	Duke 2014b
Angelica sinensis	dong quai	Antihepatotic	Duke 2014b
Arctium lappa	greater burdock	Top 10 Botanical Medicines for HCV	Buhner 2000
Arnebia euchroma	arnebia	AntiHCV	PMID12767467
Artemisia absinthium	wormwood	AntiHCV	Duke 2014b
Artemisia annua	sweet Annie	AntiHCV	PMID18699744
Astragalus membranaceous	huang qi	10 Major Immune Tonics for HCV	Buhner 2000
Betula spp.	birch	AntiHCV	PMID16250596
Boswellia carterii or	frankincense	AntiHCV;	PMID11054840

Boswellia sacra		HCV protease inhibitor via methanol extract IC90=100ug/ml	
Bupleurum spp.: *B.chinensis, B. falcatum, B. fruticosum, B. kaoi*	chai hu	Top 10 Botanical Medicines for HCV	Buhner 2000
Camellia sinensis	tea	AntiHCV via epigallocatechin gallate (EGCG) and 7,8-benzoflavone (?-naphthoflavone)	PMID22863932
Carum carvi	caraway	AntiHCV	Duke 2014b
Ceanothus spp.	red root	10 Major Immune Tonics for HCV	Buhner 2000
Chelidonium majus	celandine	Antihepatotic	Duke 2014b
Cichorium intybus	chicory	AntiHCV	Duke 2014b
Codonopsis tangshen	dang shen, bellflower	10 Major Immune Tonics for HCV	Buhner 2000
Curcuma longa	turmeric	AntiHCV; Top 10 Botanical Medicines for HCV	Duke 2014b, PMID19577913, Buhner 2000, PMID19152370, PMID19069843, PMID18484280, PMID17569218, PMID16691314
Curcuma zanthorrhiza	temulawak, Java ginger	AntiHCV	Duke 2014b
Cynara cardunculus	artichoke	Antihepatotic	Duke 2014b
Daucus maritimus or *Daucus carota*	wild carrot	AntiHCV (seed) IC50= 8 µg/ ml	PMID21895456
Eclipta prostata	eclipta, false daisy	AntiHCV via wedelolactone, luteolin, apigenin	Duke 2014b, PMID11599347l, PMID16406413, PMID18061418
Elettaria cardamomum	cardamom	AntiHCV	Duke 2014b
Eleutherococcus senticosus	eleuthero (Siberian) ginseng	10 Major Immune Tonics for HCV	Buhner 2000
Embelia schimperi	false black pepper	HCV protease inhibitor via embelin IC50=24ug/ml; HCV protease inhibitor via 5-O-methylembelin IC50=46 uM; HCV protease inhibitor via methanol extract IC90=100ug/ml	PMID11054840
Eupatorium perfoliatum	boneset	10 Major Immune Tonics for HCV	Buhner 2000
Excoecaria agallocha	buta-buta, blind-your-eye	NS3-4A protease inhibitor via excoecariphenol-D, corilagin, geraniin, chebulagic acid IC50= 3.45-9.03 uM	PMID22196120
Ficus fistulosa	common yellow-stemmed fig	AntiHCV leaf extract IC50=5.7-15.0ug/ml	PMID24089993
Flueggea virosa	common bushweed	AntiHCV via terpenoids	PMID24400834
Fumaria officinalis	fumitory	Antihepatotic	Duke 2014b

Galanthus nivalis	snowdrop	AntiHCV	PMID21599979
Ganoderma lucidum	ling zhi, reishi mushroom 10 Botanical Medicines for HCV	AntiHCV; Top	Duke 2014b, Buhner 2000
Glycyrrhiza glabra or *Glycyrrhiza* spp.	licorice	10 Major Immune Tonics for HCV; AntiHCV via glycycoumarin IC50=8.8ug /ml, glycyrin IC50=7.2ug/ml, glycyrol IC50=4.6ug/ml, liquiritigenin IC50=16.4ug/ml, glycyrrhizin, licochalcone-A IC50=2.5ug/ml, glabridin IC50=6.2ug/ml, and isoliquiritigenin IC50=3.7ug/ml	Buhner 2000, Duke 2014b, PMID24397541
Gracilaria tenuistipitata	red algae	AntiHCV via COX-2 inhibitor	PMID23469054
Haronga madagascariensis	haronga	Antihepatotic	Duke 2014b
Harpagophytum procumbens	devils' claw	Antihepatotic	Duke 2014b
Humulus lupulus	hops	AntiHCV via xanthohumol	PMID23669332
Hypericum perforatum	St. Johns-wort	AntiHCV via hypericin	PMID25301586
Hyssopus officinalis	hyssop	AntiHCV	Duke 2014b
Ligustrum lucidum	Chinese privet	AntiHCV (fruit)	PMID17531344
Lonicera japonica	Japanese honeysuckle	Antihepatotic	Duke 2014b
Marrubium vulgare	horehound	AntiHCV	Duke 2014b
Matricaria recutita	chamomile	AntiHCV	Duke 2014b
Melanolepis multiglandulosa	alim	AntiHCV via stem extract IC50= 6.2-17.1ug/ml	PMID24089993
Melicope latifolia	melicope	AntiHCV via leaf extract IC50=2.1-3.5ug/ml	PMID24089993
Mentha arvensis	field mint	Antihepatotic	Duke 2014b
Mentha x *piperita*	peppermint	Antihepatotic	Duke 2014b, PMID17371529
Morinda citrifolia	noni	AntiHCV via methanol extract IC50=20.6ug/ml; AntiHCV via n-hexane extract IC50=6.1ug/ml; AntiHCV via ethyl acetate leaf extract IC50=6.6ug/ml; AntiHCV via pheophorbide IC50 = 0.3ug/ml CC50=10ug/ml SI=33 and pyropheophorbide-a IC50 = 0.2ug/ml; CC50= 7.2ug/mL, SI=36	PMID24438164
Nigella sativum	black cumin	AntiHCV in patients ineligible for IFN/ ribavirin at 450 mg/day for 3 months	PMID23674855
Orthosiphon aristatus	Java tea	AntiHCV	Duke 2014b, PMID17265556
Osbeckia aspera	rough small-leaved spider flower	AntiHCV; Hepatoprotective	PMID11585686
Panax ginseng	oriental ginseng	Antihepatotic; 10 Major Immune Tonics for HCV	Duke 2014b, Buhner 2000

Panax notoginseng	Tienchi ginseng, san qi	10 Major Immune Tonics for HCV	Buhner 2000
Parthenium hispidum	wild quinine	AntiHCV via 1-alpha-hydroxy-11(13)-pseudoguaien-6 beta,12-olides IC90=2uM	PMID17291045
Peumus boldus	boldo	AntiHCV; Top 10 Botanical Medicines for HCV	Duke 2014b, Buhner 2000 PMID12747739, PMID19145575, Buhner 2000
Phyllanthus spp.: *P. niruri, P. amarus, P. emblica*	leafflower, stone breaker, carry-me seed	AntiHCV; Antihepatotic *(P. nururi)*; AntiHCV via root and eaf extract (*P. amara*); Top 10 Botanical Medicines for HCV	PMID21440018, Duke 2014b, Buhner 2000
Picrorhiza kurroa	kutki	Top 10 Botanical Medicines for HCV	Buhner 2000
Pimpinella anisum	anise	AntiHCV	Duke 2014b
Piper cubeba	cubeb, tailed pepper	HCV protease inhibitor via aqueous extract IC90=100ug/ml	PMID11054840
Platycodon grandiflorus	common balloon flower (root)	AntiHCV via aqueous extract; AntiHCV via triterpenoid saponins (deapioplatycodin-D, deapioplatycodin-D2, platycodin-D, platycodin-D2, platycodin-D3, platyconic acid-A) and PG saponin mixture (PGSM)	PMID22878389, PMID24489585
Poncirus trifoliata	trifoliate orange	AntiHCV	PMID12767467
Portulaca oleracea	purslane	AntiHCV via methanolic and ethyl acetate extracts	PMID25871297
Quercus infectoria	Aleppo oak	HCV protease inhibitor via methanol extract IC90=100ug/ml	PMID11054840
Rehmannia glutinosa	di huang	Antihepatotic	Duke 2014b
Rheum palmatum	Chinese rhubarb	Antihepatotic	Duke 2014b
Rosmarinus officinalis	rosemary	AntiHCV	Duke 2014b, PMID19918713
Ruta spp.: *R. angustifolia, R. chalepensis, R. graveolens*	rue	AntiHCV via arborinine (leaves) IC50=5.7-7.1ug/ml, chalepin IC50=1.2-2.2ug/ml, gamma-fagarine IC50=20.0-20.8ug/ml, kokusaginine I C50=4.8-8.0ug/ml, and pseudane-IX IC50=1.2-1.6ug/ml; AntiHCV compared to ribavirin IC50=2.4-3.2ug/ml	PMID25454460
Salvia miltiorrhiza	red root sage	Antihepatotic	Duke 2014b
Santalum album	sandalwood	Antihepatotic	Duke 2014b
Schisandra chinensis	schisandra, magnolia vine (fruit)	Antihepatotic; AntiHCV via gomosin-A; Hepatoprotective; 10 Major Immune Tonics for HCV	Duke 2014b, PMID11154048, Buhner 2000
Scutellaria baicalensis	Baikal skullcap	Antihepatotic; Top 10 Botanical Medicines for HCV	Duke 2014b, Buhner 2000

Silybum marianum	milk thistle	Antihepatotic; AntiHCV via flavonolignans, silibinin, and silymarin; Top 10 Botanical Medicines for HCV	Duke 2014b, PMID23673225, PMID23701235, Buhner 2000
Solanum nigrum	black nightshade	AntiHCV via methanol extract IC>37 and chloroform extract IC=>50	PMID21247464
Stylogne cauliflora	Peruvian stylogne	AntiHCV via oligophenol SCH 644342/644343 IC50=0.3 uM; NS3 protease inhibitors	PMID14611859
Swietenia macrophylla	mahogany	AntiHCV via 3-hydroxy caruilignan-C EC50= value of 9.3=11.7 uM; synergic with interferon or telaprevir via 2' -C-methylcytidine	PMID22497816
Syzygium aromaticum	clove	AntiHCV	PMID17380552
Taraxacum officinale	dandelion	Top 10 Botanical Medicines for HCV	Buhner 2000
Thlaspi arvense	field pennycress	AntiHCV	PMID12767467
Toona sureni	Indonesian mahogany, suren toon	AntiHCV (leaves) IC50-2.0-13.9ug/ml	PMID24089993
Trachyspermum ammi	ajowan caraway, bishop's weed	HCV protease inhibitor via methanol extract IC90=100ug/ml	PMID11054840 PMID11054840
Withania somnifera	ashwagandha	10 Major Immune Tonics for HCV	Buhner 2000

**IC = inhibitory concentration, the lowest concentration of a 90% or 50% antimicrobial extract that will inhibit the visible growth of a microorganism in overnight incubation, expressed in micrograms per milliliter (ug/ml) or micromolar (uM) concentration*

Table 2. AntiHCV Formulations

Formulation	Notes	Citation
Abnoba-viscum Quercus (AQ)	AntiHCV via *Viscum* lectins, showing a biochemical or virologic response in up to 40% of patients with chronic HCV (compare to interferon-plus-ribavirin therapy, which is effective in less than 50% of patients)	PMID11669085
Bing Gan (decoction) + interferon-α	AntiHCV; Hepatoprotective; better at clearance of viral RNA and normalizing ALT compared to interferon alone	PMID11687177
Ninjin-youei-to (Ginseng combination TJ-108 or Ren Shen Yang Rong)	AntiHCV via gomisin-A, Hepatoprotective.	PMID11154048
Sho-saiko-to (SST, aka Minor Bupleurum or Xiao Chai Hu)	AntiHCV but seems to induce pneumonitis in humans, with cough, dyspnea, fever, hypoxia (sometimes fatal)	PMID9212662, PMID10707545
Yi Zhu (decoction)	AntiHCV at RNA; better at clearance of viral RNA and normalizing ALT compared to glycyrrhizin + ribavirin	PMID11687177
Yi Er Gan (decoction)	Hepatoprotective; better at normalizing ALT compared to silymarin aglucuronolactone	PMID11687177

… the combination of polyherbal TCM formulas-plus-synthetics scores better than herbs or pharmaceuticals alone for HCV.

Peumus boldo (boldo) in flower

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Whenever I see a Cochrane Review study, I don't expect it will promote herbal medicines as compared to pharmaceuticals. So I'm not surprised by the conclusions of the Cochrane Hepato-Biliary Group that there is no firm evidence of efficacy of any medicinal herbs for HCV infection. The review says "herbs were associated with adverse events" and should not be used outside randomized clinical trials, while neglecting to mention any adverse events for ribavirin or interferon (Liu et al. 2001). Supporters of synergy between herbs and synthetics, however, might be pleased that in this Cochrane review, the combination of polyherbal TCM formulas-plus-synthetics scores better than herbs or pharmaceuticals alone for HCV.

For example, practitioners of Japanese Kampo medicine have noted that their formulas can be as effective as interferon therapy for HCV. In one short-term and long-term study, it was shown that ninjin-youei-to (Ginseng combination TJ-108 or Ren Shen Yang Rong) was very effective. Of the three herbs in the formula – *Citrus unshiu* (satsuma/cold hardy mandarin) peel, schisandra fruit, and *Polygala tenuifolia* (yuan zhi) root – schisandra fruit was found to be most active against HCV infection in an in vitro screening. The next step, which looked at gomisin-A (the lignan component of schisandra fruit) in both in vitro and animal models, concluded that the therapeutic actions of TJ-108 are both HCV inhibiting and hepatoprotective (Cyong et al. 2000). I wonder which synthetic pharmaceuticals, if any, are better for HCV infection than the herbal combinations in Table 2?

In addition to the herbs and herbal combinations enumerated above, Table 3 lists

Schisandra chinensis (schisandra) unripe berry

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Rosa rugosa (beach rose) flower buds

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the common food and herb phytochemicals that show promising actions against HCV. I have come to believe that polyherbal "food farmacy" is the best approach to chronic diseases, often more promising and less debilitating than pharmaceuticals, more cost-effective for the American health care consumer, and better for American health overall. Our bodies readily recognize the food phytochemicals known to our ancestors of millennia or more; our bodies cannot have known the new synthetic allopathic drugs mostly synthesized in the last 100 years. What led us down the seductive synthetic route with the false promise of "better living through chemistry?" It's balderdash!

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Table 3. AntiHCV Phytochemicals

Compound	Action(s)	Citation(s)	Applicable Genera or Species
Acetyl-ursolic-acid	HCV protease inhibitor	PMID18600299 PMID23422646	*Cynomorium songaricum* (stems)
Apigenin	AntiHCV	PMID23026306	Widespread, e.g. oregano, coriander, chamomile, celery, parsley, wild lettuce, yarrow
Arborinine	AntiHCV IC50=5.7-7.1ug/ml, cf. Ribavirin AntiHCV at IC50=2.4-3.2ug/ml*	PMID25454460	*Ruta angustifolia*
7,8-Benzoflavone (alpha-naphthoflavone)	AntiHCV	PMID22863932	*Camellia sinensis*
Bergenin	AntiHCV at >1000uM; HCV protease inhibitor	PMID16329286 PMID16329286	*Bergenia, Leea, Rodgersia*
Betulin	AntiHCV	PMID21377854	*Betula* 3.2%; *Euclea* 2.2%; *Diospyros* 1.0%; *Garcinia* 0.75%; *Careya* 0.6%; *Scirpus* 0.4%; *Pterospermum* 0.4%; *Alnus, Alangium* and *Lavandula* 0.2%
Betulinic acid	AntiHCV	PMID21377854	Widespread, e.g. *Psophocarpus* 5.3%; *Diospyros* 3%; *Wormia* 2.4%; *Arbutus, Cornus, Lemaireocereus*, and *Ternstroemia* 2%
Castanospermine	AntiHCV	PMID15957923	*Castanospermum*
Casuarictin	AntiHCV	PMID20144544	*Carpinus* (PMID22669603); *Eucalyptus* (PMID11705240); *Eugenia* (PMID11345703); *Fragaria* (PMID23992396); *Juglans* (PMID18841772); *Melastoma* (PMID10408242); *Miconia* (PMID21480804); *Rosa* (PMID20144544); *Rubus* (PMID1791480; PMID18211030; PMID22229937); *Syzygium* PMID10737184)
Cephalotaxine Chalepin	AntiHCV AntiHCV IC50=1.2-2.2ug/ml, cf. Ribavirin AntiHCV at IC50=2.4-3.2ug/ml	PMID17458779 PMID25454460	*Cephalotaxus* *Ruta angustifolia*
Chebulagic acid	HCV protease inhibitor IC50=3.45-9.03uM	PMID22196120	*Anogeissus, Excoecaria agallocha, Terminalia*

Corilagin	HCV protease inhibitor IC50=3.45-9.03uM	PMID22196120	*Excoecaria, Geranium, Punica, Ricinus, Terminalia*
Curcumin	AntiHCV; HCV entry inhibitor; HCV replication inhibitor	PMID20026048 PMID22922731 PMID23903236 PMID24092864 PMID20026048 PMID22922731	*Curcuma longa* 3.9%; *Curcuma zanthorrhiza* 1%; *Curcuma zedoaria* 0.1%; possibly *Zingiber*
Deapioplatycodin-D	AntiHCV	PMID24489585	*Platycodon grandiflorum*
Deapioplatycodin-D2	AntiHCV	PMID24489585	*Platycodon grandiflorum*
3,3'-Digalloyl-procyanidin-B2	HCV protease inhibitor IC50=0.91uM	PMID17624450	*Rhodiola kirilowii*
Diosgenin	AntiHCV IC50=3uM	PMID24659884	*Trigonella* 1.9%; *Solanum* 1.2%; *Daucus* 0.9%; *Dioscorea* 0.45%
Embelin	HCV protease inhibitor IC50=21uM	PMID11054840	*Ardisia, Embelia*
Epigallocatechin gallate (EGCG)	AntiHCV	PMID22863932	*Camellia sinensis*
(-)-Epigallocatechin-3-o-gallate (EGCG)	HCV protease inhibitor IC50=8.51 uM	PMID17624450	*Rhodiola kirilowii*
(-)-Epicatechin-3-o-gallate (ECG)	HCV protease inhibitor IC50=18.55uM	PMID17624450	*Rhodiola kirilowii*
Epigallocatechin-3-gallate (EGCG)	AntiHCV IC90=50uM; HCV protease inhibitor IC50=8.51uM	PMID22105803 PMID23153661 PMID17624450	*Rhodiola kirilowii*
Eugeniin	HCV invasion inhibitor	PMID20144544	*Rosa rugosa*
Excoecariphenol-D	AntiHCV; HCV protease inhibitor IC50=3.45-9.03uM; HCV protease inhibitor	PMID16329286 PMID22196120 PMID16329286	*Excoecaria agallocha*
Gamma-fagarine	AntiHCV IC50=20.0-20.8ug/ml, cf. Ribavirin AntiHCV at IC50=2.4-3.2ug/ml	PMID25454460	*Ruta angustifolia*
Flavonoids	AntiHCV; HCV protease inhibitor 33.11-370.37uM	PMID16329286	Ubiquitous
Gallic acid ethyl esters	AntiHCV; HCV protease inhibitor	PMID16329286	Widespread
Geraniin	HCV protease inhibitor IC50=3.45-9.03uM	PMID22196120 PMID22196120	*Erythroxylum* 0.3%; *Excoecaria, Geranium, Spondias*
Glabridin	AntiHCV IC50=6.2ug/ml	PMID24397541	*Glycyrrhiza*
D-Glucose-gallated -esters	AntiHCV IC50=0.68-4.86uM; HCV protease inhibitor	PMID16329286	Fairly widespread
Glycycoumarin	AntiHCV IC50=8.8ug/ml	PMID24397541	*Glycyrrhiza*
Glycyrin	AntiHCV IC50=7.2ug/ml	PMID24397541	*Glycyrrhiza*
Glycyrol	AntiHCV IC50=4.6ug/ml	PMID24397541	*Glycyrrhiza*
Glycyrrhizin	AntiHCV	PMID24397541	*Glycyrrhiza*

Gomisin-A	AntiHCV; Hepatoprotective	PMID11154048	*Schisandra chinensis*
Homoharringtonine	AntiHCV	PMID17458779	*Cephalotaxus*
Honokiol	HCV entry inhibitor IC50 >35uM	PMID22098176	*Magnolia*
3-Hydroxy-caruilignan-C	AntiHCV IC50= 9.3=11.7uM; Synergic with interferon, 2'-C-methylcytidine, or telaprevir	PMID22497816	*Swietenia macrophylla*
5-Hydroxy-3,7-dimethoxyflavone	HCV protease inhibitor IC50 =190uM; HCVM protease inhibitor IC50=190 uM	PMID16964717	*Kaempferia galanga*
Hypericin	AntiHCV	PMID15638760	*Hypericum*
Isoliquiritigenin	AntiHCV IC50=3.7ug/ml	PMID24397541	*Glycyrrhiza*
Kokusaginine	AntiHCV IC50=4.8-8.0ug/ml, cf. Ribavirin AntiHCV at IC50=2.4-3.2ug/ml	PMID25454460	*Ruta angustifolia*
Ladaneine	HCV entry inhibitor	PMID22465429	*Artemisia, Lavandula, Marrubium, Orthosiphon, Salvia, Rosmarinus, Thymus*
Lamiridosin-A	AntiHCV IC50=2.31uM	PMID19904996	*Lamium album*
Licochalcone-A	AntiHCV IC50=2.5ug/ml	PMID24397541	*Glycyrrhiza*
Lucidone	AntiHCV IC50= 15-20uM; Heme-oxygenase-1-genic	PMID23254429	*Lindera macrocarpa*
Luteolin	AntiHCV	PMID23026306	Widespread, e.g., artichoke, basil, beets, Brussels sprouts, buckwheat, cabbage, capers, carrots, cauliflower, celery, chamomile, chives, chocolate, cucumber, cumin, fennel, flax, hawthorn, horseradish, kohlrabi, lemon, lemongrass, lettuce, olive, oregano, parsley, pepper, peppermint, perilla, pomegranate, prickly pear, rooibos, rosemary, spinach, tarragon, tea, thyme, turnip
Malonyl-ursolic-acid-hemiester	HCV protease inhibitor	PMID18600299, PMID23422646	*Cynomorium songaricum* (stem)
5-o-Methylembelin	HCV protease inhibitor IC50=46uM	PMID11054840	*Embelia*
Moracin-M	AntiHCV	PMID17948170	*Morus* (bark)
Moracin-O	AntiHCV IC50=80.8uM	PMID17948170	*Morus* (bark)
Moracin-P	AntiHCV IC50=35.6uM	PMID17948170	*Morus* (bark)
Mulberroside-C	AntiHCV	PMID17948170	*Morus* (bark)
Myriberine-A	AntiHCV	PMID23320525	*Myrioneuron faberi*

Naringenin	AntiHCV IC50=109uM	PMID18393287 PMID24659884	*Citrus* (pericarp) 4.5%; *Lippia, Artemisia, Anacardium, Camellia, Centaurea* and such familiar foods as cherry, grapefruit, licorice, marjoram, milk thistle, mung bean, oregano, parsley, peach, tarragon, tea, tomato
Nobiletin (3',4',5,6,7,8-hexamethoxyflavone)	AntiHCV	PMID15844836	*Citrus* (pericarp)
Oleanolic-acid	AntiHCV; HCV entry inhibitor	PMID23662817	Widespread, e.g. *Syzygium* 2%; *Rosmarinus* 1%; *Thymus* 0.6%; *Salvia* and *Lavandula* 0.5%; *Ocimum* 0.1%
Oxymatrine	AntiHCV	PMID12650784	*Sophora flavescens*
Penta-o-galloyl-beta-D-glucoside	AntiHCV IC50=1.6uM; HCV protease inhibitor IC50=1.6uM	PMID16329286 PMID15546725	*Cornus, Eucalyptus, Euphorbia, Phyllagathis, Sapium, Terminalia* *Cornus, Eucalyptus, Euphorbia, Phyllagathis, Sapium, Terminalia*
Phaeophorbide	AntiHCV IC50 = 0.3ug/ml	PMID24438164	*Morinda citrifolia*
Pheophytin-A	HCV protease inhibitor	PMID19450556	*Lonicera*
Platycodin-D	AntiHCV	PMID24489585	*Platycodon grandiflorum*
Platycodin-D2	AntiHCV	PMID24489585	*Platycodon grandiflorum*
Platycodin-D3	AntiHCV	PMID24489585	*Platycodon grandiflorum*
Platyconic-acid-A	AntiHCV	PMID24489585	*Platycodon grandiflorum*
Proanthocyanidin	AntiHCV	PMID19531480	*Vaccinium* (leaf)
Procyanidin-B1	AntiHCV IC50=15uM	PMID20710064	*Cinnamomum* and others
Pseudoguaianolide [1alpha-hydroxy-11(13)-pseudoguaien-6beta, 12-olides]	AntiHCV IC90=2uM	PMID17291045	*Parthenium hispidum*
Pseudane-IX	AntiHCV IC50=1.2-1.6ug/ml, cf. Ribavirin AntiHCV at IC50=2.4-3.2ug/ml	PMID25454460	*Ruta angustifolia*
Pyropheophorbide-A	AntiHCV IC50 = 0.2ug/ml	PMID24438164	*Morinda citrifolia*
Quercetin	HCV protease inhibitor	PMID22239530 PMID24659884	Ubiquitous in higher plants
Quercetin-3-galactoside (hyperoside)	AntiHCV NS3-4A helicase; AntiHCV NS3-4A protease	PMID24391361	*Drosera, Stachys, Prunella, Rumex, Cuscuta, Hypericum*
Quercetin-3-glucoside (isoquercitin)	AntiHCV NS3-4A helicase; AntiHCV NS3-4A protease	PMID24391361	*Mangifera, Rheum*
Rapanone	Antihepatotic IC50=7uM; HCV protease inhibitor IC50=7uM	Duke 2014b	*Ardisia*

Rhodisin (3,3'-digalloyl-proprodelphinidin-B2)	HCV protease inhibitor IC50=0.77uM	PMID17624450	*Rhodiola kirilowii*
Rutin-gallated-esters	AntiHCV IC50=0.68-4.86uM; HCV protease inhibitor	PMID16329286	Widespread
Shikonin	AntiHCV	PMID21984340	*Arnebia, Lithospermum, Rehmannia*
Silibinin	AntiHCV	PMID23701235	*Silybum marianum*
Silibin	AntiHCV	PMID11687177 PMID18771667	*Silybum marianum*
Silymarin	AntiHCV	PMID17484885 PMID19048676 PMID19782083 PMID21083592 PMID21453551 PMID22058086 PMID23701235	*Silybum marianum*
Tellimagrandin-I	HCV invasion inhibitor	PMID20144544	*Rosa rugosa*
Tetra-o-galloyl-beta-D-glucose	HCV protease inhibitor IC50=0.75uM	PMID15546725	*Cornus, Eucalyptus, Euphorbia, Phyllagathis, Sapium, Terminalia*
Toosendanin	AntiHCV	PMID21444704	*Melia*
Tri-o-galloyl-beta-D-glucose	HCV protease inhibitor IC50=1.89uM	PMID15546725	*Cornus, Eucalyptus, Euphorbia, Phyllagathis, Rheum, Rhus, Sapium, Tamarix, Terminalia*
Ursolic-acid	HCV protease inhibitor	PMID18600299 PMID23422646	Widespread, e.g., *Salvia* 7.4%; *Nerium* (poisonous) 4.3%; *Rosmarinus* 4.1%; *Vinca* 3.7%; *Lavandula* and *Thymus* 1.9%; *Satureja* 1.6%; *Prunus* 1%
Wedelolactone	AntiHCV	PMID23026306	*Eclipta, Wedelia*
Xanthohumol	AntiHCV	PMID14670594 PMID19748253 PMID23669332	*Humulus*

**IC = inhibitory concentration, the lowest concentration of a 90% or 50% antimicrobial extract that will inhibit the visible growth of a microorganism in overnight incubation,expressed in micrograms per milliliter (ug/ml) or micromolar (uM) concentration.*