

Challenge Hepatitis C with Herbs as Drugs

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Abstract

Hepatitis C Virus (HCV) is a major concern for most of the hepatocellular carcinoma (HCC). At present, standard therapy followed is pegylated interferon α with ribavirin but it has significant side effects and was moderately effective. Therefore, there is a necessity to introduce new drugs that interact various stages of HCV life cycle. Several herbs have been isolated for treating against HCV, and are effective in preventing HCV viral diseases. Our review précises about various mode of action of certain herbs that showed inhibition activity against HCV.

Keywords: Anticarcinogenic; Artemisinin; Traditional remedies

Introduction

Treating liver disease with herbs has a long tradition especially in both Asian and European medicine. Though herbal extracts promoted for gastrointestinal or biliary disorders contain potent alkaloids that are harmful, they are also recognized for disease elimination with proven antioxidative, antifibrotic, antiviral, or anticarcinogenic properties [1]. According to the WHO, the number of people infected with hepatitis C virus has exceeded 220 million and still exploding enormously, though the cure in current medicine is the standard therapy of interferon and ribavirin [2]. The success behind these therapies is less than 50% and at most times its unaffordable [2]. Fighting back HCV with herbs as drug is a ray of hope for patients who are unable to tolerate the treatment, unaffordable or else not eligible for the current interferon and ribavirin therapy. The key differences between traditional and modern medicine is the knowledge about its protection, formulation, regulation, testing, dosage, consultation as well as training required for it. Modern medicines derived from natural products, many of which were first used in traditional remedies such as etoposide (derived from mandrake plant) and vinca alkaloids (derived rosy periwinkle) are used as anticancer drugs and originally known for various remedies in Chinese, Japanese as well as India. Artemisinin (derived from sweet wormwood) and quinine (cinchona tree) are famous antimalarial drugs, a very traditionally remedies used for treating fevers and shivers. *Cromoglycate* (khella plant), *hirudin* (leeches), *lovastatin* (mushroom and red yeast rice), *opiates* (unripe poppy seeds) are known for their herbal action such as asthma, anticoagulant, lower cholesterol and analgesics and are originally used as remedies in Egypt, China, Japan, Eastern Europe, India and North Africa.

But determining whether herbal remedies are effective and safe for hepatitis C will be a step high to take a more traditional approach to their research. Current techniques have facilitated researchers to discover active compounds of herbs as antiviral agents. Among the herbs against HCV core, glycyrrhizin inhibited the activity of the core protein at protein level and mRNA [3,4] as well as Silybum marianum

was tested by western blotting inhibiting HCV core protein [5]. Our in silico study targeting the HCV cores from India, have shown flavonoid components EGCG followed by silybin and naringenin has best interaction to collide the core residues [6]. Methanolic and chloroform extracts from *Quercus infectoria*, *Boswellia carterii*, *Embelia schimperi*, *Trachyspermum ammi*, *Syzygium aromaticum*, *Piper cubeba* and *Acacia nilotica* are known to target against NS3 protease [7]. Recently *Viola yedoensis* is investigated and isolated coumarins have significantly inhibited NS3/4A protease thereby serving as a template for antiviral drugs [8]. One of our in silico inhibition of HCV NS3 helicase has shown better interaction with flavonoids quercetin and catechins [9] and also its reported fluoroquinolones inhibit HCV replication possibly by targeting the HCV NS3 helicase [10]. *Amelanchier alnifolia* derived flavonoids is known to be potential inhibitors of active site of NS3/4 protease and helicase [11]. Quercetin is considered as an anti-HCV agent is not only reduced by IRES activity its augmentation by NS5A, thereby reducing viral protein synthesis without any toxic effects [12]. Extract from *Eclipta alba* and its isolates were studied for their capability to inhibit activity of HCV replicase (HCV NS5B) in vitro as well replication of HCV in a cell culture system having replicating HCV subgenomic RNA replicon [13]. Bioassay-based fractionations of the extracts luteolin apigenin and Wedelolactone, revealed dose dependent inhibition of HCV replicase in vitro as well in the cell culture system [13]. *Ruta angustifolia* leaves was tested for antiviral activities against HCV in cell culture and its isolated compounds chalepin and pseudane IX inhibited HCV at the post-entry step and decreased the levels of HCV RNA replication and viral protein synthesis NS5A [14]. Study showed persuasive inhibition of luteolin against NS5B polymerase activity [15].

We have tested few herbal compounds in silico and we are taking them in vitro so we can really know if there is any benefit and it can be possible that in the near future some of these herbal therapies may actually benefit patients from HCV. We conclude saying there is broad action of natural herbs as potential HCV antivirals, though many natural compounds don't target directly be used to develop the current HCV therapy. All though a large number of these natural compounds are available which can be screened through variety of in silico

approaches that can test for anti-HCV activities and subsequently taking it into in vitro inhibition activity of a viral protein does not only finally validate that this viral protein is the proper target but further research are clearly necessary to confirm these molecules *in vivo*.

In conclusion, even if we do not presume that herbs may replace the present anti-HCV therapy, treatments can more likely improved, and perhaps lightened by limiting their cost, improved diet and thereby

challenging HCV through an alternative source. Therefore when we are living with a disease infected with hepatitis C, it is natural to want to try any treatment possible to relieve from the disease and improve the quality of life. If both developed and developing countries unite research capacities in equitable collaborations, new scientific methodologies could trigger a revival in global health research and development.

Viral Proteins	Herbal plants	Mode of action	Tested	Combination therapy/dose concentration	References
Core	<i>Glycyrrhizin (GL)</i>	Inhibition in mRNA and protein level	Genotype 3a (55 samples)	Administered with interferon	[16]
	<i>Silybum marianum (SM)</i>	Inhibiting the core expression, suppressed activity of core protein, assembly of HCV particles.	Genotype 3a	Combination with interferon, combination of two diastereoisomers	[17,18]
	<i>Naringenin</i>	Inhibit apolipoprotein B-dependent secretion of HCV particles, inhibits the microsomal triglyceride transfer protein activity as well as the transcription of 3-hydroxy-3-methyl-glutaryl-coenzyme A reductase and acyl-coenzyme A:cholesterol acyltransferase 2 in infected cells	Huh 7 cells	Dose concentration of 200 M	[19]
E1	<i>Epigallocatechin-3-gallate (EGCG) Lamium album</i>	Inhibiting HCV entry, inhibit HCV replication via cyclooxygenase-2 pathway, disturbing the contact of HCV envelope 2 proteins (E2) with the CD81 receptor	Cell-culture-derived HCV (HCVcc) HCVpp	Dose concentration of 50 IM containing lamiridosins A/B (1/2) and iridoids aglycone epimers	[23]
E2	<i>Ladanein (BJ486K)</i>	Post attachment entry step of HCV, inhibitor against scavenger receptor class B type I	Mice	Combination with cyclosporine	[24]
p7	<i>Epigallocatechin-3-gallate (EGCG)</i>	Cell to cell spread	Cell-culture-derived HCV (HCVcc)	Not Available	[20,25]
NS2	<i>Proanthocyanidin (blueberry)</i>	Suppresses HCV replication, possibly by interacting with hnRNP A2/B	HCV subgenome in replicon cells	Not Available	[25]
NS3	<i>Boswellia carterii, Acacia nilotica, Quercus infectoria, Embelia schimperi, Trachyspermum ammi, Q. infectoria, Piper cubeba and Syzygium aromaticum</i>	Blocks replication by targeting the NS3 protease, restored IRF-3 phosphorylation	Huh 7 cells	Dose concentration of 100 µg/ml	[26]
	<i>Solanum nigrum (SN), Viola yedoensis</i>	Solanum nigrum (SN), Viola yedoensis	Huh 7 cells	Dose concentration of 0.5 µg/ml	[8,27]
NS4A	<i>Ellagitannins, punicalagin, punicalin, and ellagic acid, Quercetin, Accacia nilotica</i>	Inhibition of the enzyme activity	Cell-culture-derived HCV (HCVcc)	NA	[28,29]
NS4B	<i>Curcumin (turmeric)</i>	Reduced the HCV replication, suppressing the AKT SREBP-1 pathway	Cell-culture-derived HCV (HCVcc)	Dose concentration of 18.2 µM	[30]

	<i>Quercetin</i>	Inhibit HCV by targeting the cellular heat shock proteins, HSPs 40 and 70	Cell-culture-derived HCV (HCVcc)	HCV	Dose concentration of 50 µm	[12]
NS5A	<i>Silibinin</i>	Inhibition in mRNA a level, reduced IRES activity	Cell-culture-derived HCV (HCVcc)	HCV	Dose concentration of 75–100 µM and 40–85 µM	[31,32]
NS5B	<i>Luteolin</i> <i>Silibinin</i>	Inhibition of NS5B polymerase activity	Genotype 3a (60 samples)		Dose concentration of 75–100 µM	[15,33]

Table 1: Mode of action of certain herbs that showed inhibition activity against HCV.

Conflict of Interest

All authors disclose no conflict of interest.

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