

infection (19). Interferon-alpha is abbreviated as both IFN-alpha and IFN-alfa. Proposed mechanisms of ribavirin are:

- Ribavirin promotes signaling by interferon, thereby enhancing interferon's effects against HCV (20,21). Microarray analyses demonstrated that ribavirin increases induction of interferon-stimulated genes.
- Ribavirin inhibits the enzyme, inosine monophosphate dehydrogenase (22). This is a key enzyme in the biosynthesis of nucleotides (23). This inhibition results in depletion of intracellular guanosine pools (pools needed for viral replication).
- Ribavirin may provoke mutations in the viral genome, where the result of the mutations is termination of the viral lifecycle. A study of human subjects treated for 1 year with ribavirin plus interferon showed an increase in mutations in the HCV genome, for example, C → U and G → A mutations (24). But in a 24-week study of human subjects with chronic HCV infection, Chevaliez et al. (25), determined that ribavirin monotherapy (or ribavirin plus IFN-alpha) did not influence HCV's mutation rate.

Although treatment of HCV involves ribavirin in combination with one or more other drugs such as pegylated IFN-alfa-2, an effort has been to eliminate both of these drugs because of their adverse effects. IFN-alfa-2 is a naturally occurring cytokine, but when used as a drug, it is chemically modified by attaching polyethylene glycol (PEG). PEG is an inert polymer that, when covalently attached to the interferon, increases its half-life in the bloodstream. Thus, the drug is called, "pegylated IFN-alfa-2."

The majority of acute HCV infections become chronic. Until the year 2011, the only approved therapies for chronic HCV were those that included IFN-alfa-2. The success rates of these IFN-alfa-2-based therapies ranged from 40% to 90% depending on the genotype of the infecting virus (26). In 2011, two small-molecule drugs, boceprevir and telaprevir, which act directly on HCV-encoded proteins, were approved by the FDA.

Drugs against HCV also include boceprevir, telaprevir, and simeprevir. These drugs inhibit an enzyme that is encoded by the genome of this virus, namely, *NS3/4A protease*. Anti-HCV drugs also include ledipasvir, daclatasvir, and

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