

ferons such as α -, β - and γ -interferons, recombinant or naturally occurring, may be advantageously used in this invention.

[0033] This combination dose regimen is flexible, and depends on the clinical condition of the subject. Where subjects are refractory to the preferred dosage levels, these may be increased within the limits dictated by undesirable side effects. Typically, injections are made five times per week and continue until an acceptable response by the subject is realized.

[0034] Tests to determine the effectiveness of the combination therapy may be the same as those described above for thymosin treatment alone. In addition, histological examination of liver biopsy samples may be used as a second major criteria for evaluation. Knodell, R. G., et al., *Hepatology*, 1:431-5 (1981), whose Histological Activity Index (portal inflammation, piecemeal or bridging necrosis, lobular injury and fibrosis) provides a scoring method for disease activity.

[0035] The following examples are provided merely to illustrate the invention, and are not to be construed in any way as limiting the scope of invention as set forth in the specification and claims.

EXAMPLE 1

Preparation of Injectable Formulation

[0036] Pharmaceutical dosage units or 1 ml each are prepared from the ingredients shown in Table 1 below.

TABLE 1

	Amount Per mL
<u>Active Ingredient</u>	
Thymosin α -1	0.0016 g
<u>Inactive Ingredients</u>	
mannitol, U.S.P.	0.050 g
sodium phosphate dibasic, heptahydrate, U.S.P.	0.002 g
sodium phosphate monobasic, monohydrate, U.S.P.	0.0005 g
sodium phosphate dibasic, 2 mg/ml solution	
sodium phosphate monobasic, 0.5 mg/ml solution	
water for injection, U.S.P.	

EXAMPLE 2

Treatment of Hepatitis C Infections in Human Patients with Thymosins and Interferons

[0037] Adult patients with chronic active hepatitis C (CAHC) are randomized to one of four study groups, made up of about 40 patients per group. Selection criteria include: (1) patients are adults (at least 18 years of age); (2) serum ALT is elevated for at least six months prior to treatment with at least one value greater than twice the upper limit of normal in the laboratory doing the testing; (3) patients test positive for HCV antibody on two occasions and on a confirmatory test; and (4) liver biopsy within three months of treatment exhibits pathology consistent with chronic active hepatitis.

[0038] Exclusion criteria include: (1) recent use of other anti-viral or immunosuppressive medication; (2) hemophilia, pregnancy or HIV infection, or other serious illness that could prevent completion of the course of treatment; (3) other forms of liver disease, including hepatitis A or B, α -1 antitrypsin deficiency, Wilson's disease, and hemochromatosis must be absent; (4) autoimmune markers (ANA, ASMA, AMA, anti-LKMI) must be absent or, if present, titers should be $<1:40$; (5) leukocyte deficiency ($<3,000$); (6) low absolute neutrophil count ($<1,000$); (7) low platelets ($<75,000$); (8) low Hb (<11 g/dL); (9) high bilirubin (>4 mg/dL); and (10) low serum albumin (3 g/dL).

[0039] The first of the four randomized groups receives interferon, preferably interferon α -2b, at a dose of 3 million units (MU) subcutaneously (SQ) on Mondays, Wednesdays and Fridays, and receives placebos on Tuesdays and Saturdays. The second group receives the same dose/schedule of interferon, plus a thymosin, preferably THN α_1 , at a dose of 900 $\mu\text{g}/\text{m}^2$ SQ on Tuesdays and Saturdays. The third group receives the same dose/schedule of a thymosin alone. The fourth group receives placebo treatment initially, but can be randomized to the three treatment groups thereafter. Interferons and thymosins can be recombinant.

[0040] Patients begin treatment while hospitalized for about one week, during which period side-effects are monitored.

[0041] Outpatient follow-up is initially at one week intervals for two weeks, then at two week intervals for two months, and then monthly for the remainder of the treatment period. At each visit the following lab tests are performed: CBC, platelet count, differential and ESR, ALT, AST, GGT, alkaline phosphatase, bilirubin, total bilirubin/albumin and HCV antibody. At monthly intervals serum γ -globulin, TSH, ANA and ASMA are assessed.

[0042] Drug toxicity is monitored on an ongoing basis using both clinical and laboratory parameters.

[0043] Within one month of completing the initial six months of treatment, patients undergo liver biopsy for pathological examination according to Knodell et al. above. This system provides a numerical scoring system of histological activity in patients with asymptomatic CAH.

[0044] At this time, control patients are randomized into three groups to receive one of the three treatment modalities, assuming that they still have CAH on follow-up liver biopsy, and that one arm of the study does not show highly significant positive or negative results on analysis at six months.

[0045] Patients in the treatment groups are followed to evaluate recrudescence of disease as evidenced by rising ALT levels. Patients who showed response in the initial six month treatment period, but who have a recurrence of the disease thereafter, are provided with additional therapy.

[0046] Additional serum or tissue tests are performed if possible: evaluation of antibodies to interferons and thymosins, polymerase chain reaction amplification of hepatitis C genome segments in liver biopsy samples, and quantitative evaluation of anti-hepatitis; C serum titers.

EXAMPLE 3

[0047] The treatment protocol is as in Example 2, except that the interferon is used at the level of 2 MU, and the thymosin at 1050 $\mu\text{g}/\text{m}^2$.