



**RECOMBINATION SUPER COMPOUND INTERFERON USED AS HEPATITIS B
SURFACE ANTIGEN AND E ANTIGEN INHIBITOR**

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FIELD OF THE INVENTION

This invention is related to a recombinant super-compound interferon (rSIFN-co) with changed dimensional structure. The characteristic of rSIFN-co in this invention is that it cannot only inhibit DNA (deoxyribonucleic acid) duplication of the hepatitis B virus but also the secretion of HBsAg and HBeAg.

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BACKGROUND OF THE INVENTION

rSIFN-co is a new interferon molecule constructed with the most popular conservative amino acid found in natural human α -IFN subtypes using genetic engineering methods. United States Patent Nos. 4,695,623 and 4,897,471 have described it. rSIFN-co had been proved to have broad-spectrum IFN activity and virus- and tumor-inhibition and natural killer cell activity. United States Patent No. 5,372,808 by Amgen, Inc. addresses treatment rSIFN-co. Chinese Patent No. 97193506.8 by Amgen, Inc. addresses re-treatment of rSIFN-co on hepatitis C. Chinese Patent No. 98114663.5 by Shenzhen Jiusheng Bio-engineering Ltd. addresses treatment of rSIFN-co on hepatitis B and hepatitis C.

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The United States Food and Medicine Administration (FDA) authorized Amgen Ltd. to produce rSIFN-co with *E. Coli*. for clinical hepatitis C treatment at the end of 1997.

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Hepatitis B patients can be identified when detecting HBsAg and the HBeAg. α -IFN is commonly used in clinics to treat hepatitis B. IFN binds superficial cell membrane receptors, inhibiting DNA and RNA (ribonucleic acid) duplication, including inducing some enzymes to prevent duplication of the virus in hepatitis-infected cells. All IFNs can inhibit only the DNA duplication of viruses, not the e and s antigen.



DETAILED DESCRIPTION OF THE INVENTION
Invention Component

It was surprising to find that rSIFN-co, the dimensional
5 structure of which has been changed, is not only a
preparation to inhibit the DNA duplication of hepatitis B,
but to inhibit the secretion of HBsAg and HBeAg.

The objective of this invention is to offer a preparation of
10 rSIFN-co to inhibit the DNA duplication of hepatitis B
viruses and the secretion of HBeAg and HBsAg of hepatitis B
and decrease them to normal levels.

Results of this invention: The production of rSIFN-co with
15 recombinant techniques. On the condition of fixed amino acid
sequence, the IFN DNA was redesigned according to the *E. Coli*.
codon usage and then the rSIFN-co gene was artificially
synthesized.

20 rSIFN-co cDNA was cloned into the high-expression vector of *E.*
Coli by DNA recombinant techniques, and a high expression of
rSIFN-co was gained by using of induce/activate-mechanism of
L-arabinose to activate the transcription of P_{BAD} promoter.

25 Compared with usual thermo-induction, pH induction and IPTG
induction systems of genetic engineering, arabinose
induction/activation system has some advantages: (1) Common
systems relieve promoter function by creating a
"derepression" pattern. Promoters then induce downstream gene
30 expression. So temperature and pH change and the addition of
IPTG cannot activate promoters directly. In the system
disclosed herein, L-arabinose not only deactivates and
represses but also activates the transcription of P_{BAD}
promoter which induce a high expression of rSIFN-co.
35 Therefore, the arabinose induction/activation system is a
more effective expression system. (2) The relation between
Exogenous and L-arabinose dosage is linearity. This means the
concentration of arabinose can be changed to adjust the
expression level of the exogenous gene. Therefore, it is

easier to control the exogenous gene expression level in *E.coli* by arabinose than by changing temperature and pH value. This characteristic is significant for the formation of inclusion bodies. (3) L- arabinose is resourceful cheap and safe, which, on the contrary, are the disadvantages of other inducers such as IPTG.

This invention creates an effective and resistant rSIFN-co-expressing *E. Coli*. engineering strain with an L-arabinose induction/activation system. The strain is cultivated and fermented under suitable conditions to harvest the bacterial bodies. Inclusion bodies are then purified after destroying bacteria and washing repeatedly. The end result, mass of high-purity, dimensional-structure-changed rSIFN-co protein for this invention and for clinical treatment, was gained from denaturation and renaturation of inclusion bodies and a series of purification steps.

The following are some rSIFN-co preparations: tablets, capsules, oral liquids, pastes, injections, sprays, suppositories, and solutions. Injections are recommended. It is common to subcutaneously inject or vein-inject the medicine. The medicine carrier could be any acceptance medicine carrier, including carbohydrate, cellulose, adhesive, collapse, emollient, filling, add-dissolve agent, amortization, preservative, add-thick agent, matching, etc.

DETAILED DESCRIPTION OF THE FIGURE

Figure 1. DNA coding sequence and deduced amino acid sequence of rSIFN-co

EXPERIMENTAL DETAILS

Embodiment experience:

The invention disclosed herein also experimentally verifies that the dimensional-structure-changed rSIFN-co can inhibit HBV-DNA duplication and secretion of HBsAg and HBeAg.

Materials

Solvent and Dispensing Method: Add 1ml saline into each vial,

dissolve, and mix with MEM culture medium at different concentrations. Mix on the spot.

Control drugs: IFN- α 2b (Intron A) as lyophilized, purchased
5 from Schering Plough. 3×10^6 U each, mix to 3×10^6 IU/ml with
culture medium; INFERGEN (liquid solution) , purchased from
Amgen, 9 μ g, 0.3ml each, equal to 9×10^6 IU, and mix with
 9×10^6 IU/ml culture medium preserve at 4°C; 2.2.15 cell:
2.2.15 cell line of hepatoma (Hep G2) cloned and transfected
10 by HBV DNA, constructed by Mount Sinai Medical Center.

Reagent: MEM powder, Gibco American Ltd. cattle fetal blood
serum, HycloneLab American Ltd. G-418(Geneticin); MEM
dispensing, Gibco American Ltd.; L-Glutamyl, imported and
15 packaged by JING KE Chemical Ltd.; HBsAg and HBeAg solid-
phase radioimmunoassay box, Northward Reagent Institute of
Chinese Isotope Ltd.; Biograncetina, Northern China Medicine;
And Lipofectin, Gibco American Ltd.

20 Experimental goods and equipment: culture bottle, Denmark
TunclonTM; 24-well and 96-well culture board, Corning
American Ltd.; Carbon Dioxide hatching box, Shel-Lab American
Ltd.; MEM culture medium 100ml: 10% cattle fetal blood serum,
3% Glutamyl1%, G418 380 μ g/ml, biograncetina50U/ml.

25 Method:

2.2.15 cell culture: Added 0.25% pancreatic enzyme into
culture box with full of 2.2.15 cell, digest at 37°C for 3
minutes, and add culture medium to stop digest and disturb it
30 to disperse the cells, reproduce with ratio of 1:3. They will
reach full growth in 10 days.

Medicine toxicity test: In this test, set groups of different
medicine concentrations and a control group in which cell is
35 not acted on with medicine. Digest cell, and dispense to a
100,000 cell/ml solution. Inoculate to 96-well culture board,
200 μ l each well, culture at 37°C for 24h with 5% CO₂. Test
when simple cell layer grows.

Dispense rSIFN-co to 1.8×10^7 IU/ml solution than prepare a series of solutions diluted at two-fold gradients. Add into 96-well culture board, 3 wells per concentration. Change the solution every 4 days. Test cytopathic effect by microscope after 8 days. Fully destroy as 4, 75% as 3, 50% as 2, 25% as 1, zero as 0. Calculate average cell lesion and inhibition rate of different concentrations. Calculate TC50 and TC0 according to the Reed Muench method.

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$$TC50 = \text{Antilog} \left(B + \frac{50-B}{A-B} \times C \right)$$

A=log >50 % medicine concentration, B=log<50 % medicine concentration, C=log dilution power

15 Inhibition test for HBeAg and HBsAg: Separate into positive and negative HBeAg and HBsAg contrast groups, cell contrast group and medicine concentration groups. Inoculate 700,000 cells/ml of 2.2.15 cell into 6-well culture board, 3 ml each well, culture at 37°C for 24h with 5% CO₂, then prepare 5
20 gradiently diluted solutions with 3-fold as the grade (Prepare 5 solutions, each with a different protein concentration. The concentration of Solution 2 is 3 times lower than that of Solution 1, the concentration of Solution 3 is 3 times lower than that of Solution 2, etc.)
25 4.5×10^6 IU/ml, 1.5×10^6 IU/ml, 0.5×10^6 IU/ml, 0.17×10^6 IU/ml, and 0.056×10^6 IU/ml, 1 well per concentration, culture at 37°C for 24h with 5% CO₂. Change solutions every 4 days using the same solution. Collect all culture medium on the 8th day. Preserve at -20°C Repeat test 3 times to estimate HBsAg and HBeAg with
30 solid-phase radioimmunoassay box (Northward Reagent Institute of Chinese Isotope Ltd.). Estimate cpm value of each well with a γ- accounting machine.

Medicinal effects calculation: Calculate cpm mean value of
35 contrast groups and different-concentration groups and their standard deviation, P/N value such as inhibition rate, IC50 and SI.

$$1) \text{ Antigen inhibition rate (\%)} = \frac{A-B}{A} \times 100$$

A = cpm of control group; B = cpm of test group;

2) Counting the half-efficiency concentration of the medicine

5 Antigen inhibition IC50 = Antilog $(B + \frac{50-B}{A-B} \times C)$

A=log>50% medicine concentration, B=log<50 % medicine concentration, C=log dilution power

10 3) SI of interspace-conformation changed rSIFN-co effect on HBsAg and HBeAg in 2.2.15 cell culture:

$$SI = \frac{TC50}{IC50}$$

4) Estimate the differences in cpm of each dilution degree from the control group using student *t* test

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Southern blot: (1) HBV-DNA extract in 2.2.15 cell: Culture cell 8 days. Exsuction culture medium (Separate cells from culture medium by means of draining the culture medium.). Add lysis buffer to break cells, then extract 2 times with a mixture of phenol, chloroform and isoamyl alcohol (1:1:1), 10,000g centrifuge. Collect the supernatant adding anhydrous alcohol to deposit nucleic acid. Vacuum draw, re-dissolve into 20μl TE buffer. (2) Electrophoresis: Add 6X DNA loading buffer, electrophoresis on 1.5% agarose gel, IV/cm, at fixed pressure for 14-18h. (3) Denaturation and hybridization: respectively dip gel into HCl, denaturation buffer and neutralization buffer. (4) Transmembrane: Make an orderly transfer of DNA to Hybond-N membrane. Bake, hybridize and expose with dot blot hybridization. Scan and analyze relative density with gel-pro software. Calculate inhibition rate and IC50.

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Results

Results from Tables 1, 2 and 3 show: After maximum innocuous concentration exponent culturing for 8 days with 2.2.15 cell, the maxima is $9.0 \pm 0 \times 10^6$ IU/ml and the average inhibition rate

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of maximum innocuous concentration rSIFN-co to HBeAg is $46.0 \pm 5.25\%$ ($P < 0.001$), IC_{50} is $4.54 \pm 1.32 \times 10^6$ IU/ml, SI is 3.96; rate to HBsAg is $44.8 \pm 6.6\%$, IC_{50} is $6.49 \pm 0.42 \times 10^6$ IU/ml, SI is 2.77. This shows that rSIFN-co can significantly inhibit the activity of HBeAg and HBsAg, but that the IFN of the contrast group and INFERGEN cannot. It has also been proved in clinic that rSIFN-co can decrease HBeAg and HBsAg or return them to normal levels.

The following are some examples for the preparation of rSIFN-co:

Example 1: Preparation of lyophilized injection

- a) rSIFN-co 3×10^6 IU
- b) citric acid 0.2 mg
- c) dibasic sodium phosphate 2.5 mg
- d) NaCl 4.0 mg
- e) dextran 20 mg
- f) Polyoxyethelene anhydrosorbitol monoelaeo-acids ester 0.1 ml
- g) inject water to a level of 1.0 ml

Preparation technique: Weigh materials according to recipe. Dissolve with sterile and pyrogen-free water. Filter through $0.22\mu m$ membrane to de-bacterialize, preserve at $6-10^\circ C$. Fill in vials after affirming it is sterile and pyrogen-free. Add 1.0 ml solution to each bottle, and lyophilize in freeze dryer.

Example 2: Preparation of liquid injection

- a) rSIFN-co 3×10^6 IU
- b) citric acid 0.2 mg
- c) dibasic sodium phosphate 2.5 mg
- d) NaCl 4.0 mg
- e) dextran 20 mg
- f) Polyoxyethelene anhydrosorbitol monoelaeo-acids ester 0.1 ml

g) inject water to a level of 1.0 ml

Preparation technique: Weigh materials according to recipe. Dissolve with sterile and pyrogen-free water. Filter through
5 0.22µm membrane to de-bacterialize, preserve at 6-10°C. Fill in airtight vial after affirming it is sterile and non-pyrogen at 1.0 ml per vial. Store end product at 2-10°C, and protect from light.

Table 1: Results of inhibition rate of rSIFN-co to HBsAg and HBeAg

First batch: (rSIFN-co)

Inhibition effect to HBeAg										
Concentration ($\times 10^4$ IU/ml)	First well	Second well	Third well	Inhibition rate			Average inhibition rate	Accumulation	1- Accumulation	Accumulated inhibition rate
				First well	Second well	Third well				
900	9026	8976	10476	0.436227	0.43935	0.345659	0.407079	0.945909	0.592921	0.614693546
300	9616	12082	10098	0.3993754	0.245347	0.369269	0.337997	0.5388299	1.254924	0.300392321
100	9822	16002	12800	0.386508	0.0005	0.2005	0.195836	0.200833	2.059088	0.08867188
33.33333	15770	19306	16824	0.014991	0	0	0.004997	0.0049969	3.054091	0.001633453
11.11111	19172	22270	18934	0	0	0	0	0	4.054091	0
Control	Cell	16010		Blank	0		Dilution	3	IC50	602.74446016
Inhibition effect to HBsAg										
Concentration ($\times 10^4$ IU/ml)	First well	Second well	Third well	Inhibition rate			Average inhibition rate	Accumulation	1- Accumulation	Accumulated inhibition rate
				First well	Second well	Third well				
900	7706	7240	7114	0.342155	0.381936	0.392693	0.372261	0.922258	0.627739	0.595006426
300	8856	7778	9476	0.2439816	0.336008	0.191053	0.257014	0.5499972	1.370724	0.286349225
100	10818	10720	10330	0.07649	0.084856	0.118149	0.093165	0.292983	2.27756	0.113977019
33.33333	10744	11114	10570	0.082807	0.051221	0.097661	0.07723	0.1998179	3.20033	0.058767408
11.11111	10672	9352	10810	0.088953	0.201639	0.077173	0.122588	0.122588	4.077742	0.02918541
Control	Cell	11714		Blank	0		Dilution	3	IC50	641.7736749

Second batch: (rSIFN-co)

Inhibition effect to HBeAg										
Concentration ($\times 10^4$ IU/ml)	First well	Second well	Third well	Inhibition rate			Average inhibition rate	Accumulation	1- Accumulation	Accumulated inhibition rate
				First well	Second well	Third well				
900	7818	8516	9350	0.554378	0.514592	0.467054	0.512008	1.371181	0.487992	0.737521972
300	10344	10628	9160	0.4103967	0.394209	0.477884	0.427497	0.8591731	1.060496	0.447563245
100	12296	14228	13262	0.299134	0.18901	0.244072	0.244072	0.4316522	1.816423	0.19201839
33.33333	15364	17414	16188	0.124259	0.00741	0.77291	0.069653	0.1876045	2.74677	0.063933386
11.11111	17386	13632	15406	0.009006	0.222982	0.121865	0.117951	0.117951	3.628819	0.03148073
Control	Cell	16962		Blank	0		Dilution	3	IC50	365.9357846
Inhibition effect to HBsAg										
Concentration ($\times 10^4$ IU/ml)	First well	Second well	Third well	Inhibition rate			Average inhibition rate	Accumulation	1- Accumulation	Accumulated inhibition rate
				First well	Second well	Third well				
900	5784	6198	5792	0.498265	0.462353	0.497571	0.486063	0.893477	0.513937	0.634835847
300	7150	8534	8318	0.379771	0.259715	0.278452	0.30598	0.4074138	1.207957	0.252210647
100	9830	11212	10210	0.147294	0.027412	0.11433	0.096345	0.101434	2.111612	0.04583464
33.33333	13942	12368	13478	0	0	0	0	0.0050891	3.111612	0.001632835
11.11111	12418	11634	11352	0	0	0.015267	0.005089	0.005089	4.106523	0.001237728
Control	Cell			Blank	0		Dilution	3	IC50	611.0919568

Third batch: (rSIFN-co)

Inhibition effect to HBeAg								
Concentration ($\times 10^4$ IU/ml)	First well	Second well	Third well	Inhibition rate			Average inhibition rate	Accumulation
				First well	Second well	Third well		
900	9702	9614	8110	0.428016	0.433204	0.52187 2	0.461031	1.316983
300	8914	10032	8870	0.4744723	0.40856	0.47706 6	0.453366	0.8559525
100	16312	12688	13934	0.038321	0.251975	0.17851 7	0.156271	0.402586
33.33333	15080	12814	13288	0.110954	0.244547	0.21660 2	0.190701	0.2463153
11.11111	21928	15366	15728	0	0.094093	0.07275 1	0.0055615	0.055615
Control	Cell	17544		Blank	0		Dilution	3
								IC50
								382.0496935

Inhibition effect to HBsAg

Inhibition effect to HBsAg								
Concentration ($\times 10^4$ IU/ml)	First well	Second well	Third well	Inhibition rate			Average inhibition rate	Accumulation
				First well	Second well	Third well		
900	5616	6228	5346	0.496864	0.442035	0.52105 4	0.486651	0.763125
300	8542	8590	7096	0.234725	0.230425	0.36427 2	0.276474	0.2764738
100	11420	11360	11394	0	0	0	0	0
33.33333	12656	11582	13110	0	0	0	0	0
11.11111	13142	12336	13342	0	0	0	0	0
Control	Cell	11528		Blank	0		Dilution	3
								IC50
								694.7027149

HBeAg: Average IC50: 450.2434 SD: 132.315479

HBsAg: Average IC50: 649.1894 SD: 42.29580

Table 2: Results of inhibition rate of Intron A(IFN-α2b) to HBsAg and HBeAg

Inhibition effect to HBeAg										
Concentration ($\times 10^4$ IU/ml)	First well	Second well	Third well	Inhibition rate			Average inhibition rate	Accumulation	1- Accumulation	Accumulated inhibition rate
				First well	Second well	Third well				
300	14918	11724	9950	0	0.029711	0.176529	0.068747	0.068747	0.931253	0.068746724
100	14868	16890	15182	0	0	0	0	0	1.931253	0
33.33333	16760	21716	16400	0	0	0	0	0	2.931253	0
11.11111	20854	15042	16168	0	0	0	0	0	3.931253	0
3.703704	12083	12083	12083	0	0	0	0	0	4.931253	0
Control	Cell	17544		Blank	0		Dilution	3	IC50	FALSE
Inhibition effect to HBsAg										
Concentration ($\times 10^4$ IU/ml)	First well	Second well	Third well	Inhibition rate			Average inhibition rate	Accumulation	1- Accumulation	Accumulated inhibition rate
				First well	Second well	Third well				
300	9226	8196	9658	0.152489	0.247106	0.521054	0.1708	0.189295	0.8292	0.185857736
100	10946	10340	10828	0	0.050156	0.364272	0.018495	0.0184947	1.810705	0.010110817
33.33333	12250	12980	13934	0	0	0	0	0	2.810705	0
11.11111	12634	12342	12000	0	0	0	0	0	3.810705	0
3.703704	10886	10886	10886	0	0	0	0	0	4.810705	0
Control	Cell	10886		Blank	0		Dilution	3	IC50	FALSE

Table 3: Results of inhibition rate of Infergen to HBsAg and HBeAg
First batch: (Infergen)

Inhibition effect to HBeAg										
Concentration ($\times 10^4$ IU/ml)	First well	Second well	Third well	Inhibition rate			Average inhibition rate	Accumulation	1- Accumulation	Accumulated inhibition rate
				First well	Second well	Third well				
900	14172	12156	17306	0.091655	0.220869	0	0.104175	0.306157	0.895825	0.254710274
300	13390	12288	16252	0.1417767	0.212409	0	0.118062	0.2019827	1.777764	0.102024519
100	14364	18834	14194	0.079349	0	0.090245	0.056531	0.083921	2.721232	0.029916678
33.33333	15722	16034	16340	0	0	0	0	0.0273897	3.721232	0.007306592
11.11111	17504	17652	14320	0	0	0.082169	0.02739	0.02739	4.693843	0.005801377
Control	Cell	15602		Blank	0		Dilution	3	IC50	FALSE
Inhibition effect to HBsAg										
Concentration ($\times 10^4$ IU/ml)	First well	Second well	Third well	Inhibition rate			Average inhibition rate	Accumulation	1- Accumulation	Accumulated inhibition rate
				First well	Second well	Third well				
900	12080	11692	12234	0	0.01275	0	0.00425	0.025163	0.99575	0.024647111
300	12840	11484	12350	0	0.030313	0	0.010104	0.0209125	1.985646	0.010422073
100	12894	14696	15086	0	0	0	0	0.010808	2.985646	0.003606955
33.33333	15032	12928	13020	0	0	0	0	0.0108081	3.985646	0.002704416
11.11111	11794	11984	11508	0.004137	0	0.028287	0.010808	0.010808	4.974837	0.002167838
Control	Cell	11843		Blank	0		Dilution	3	IC50	FALSE

Second batch: (Infergen)

Inhibition effect to HBeAg										
Concentration ($\times 10^4$ IU/ml)	First well	Second well	Third well	Inhibition rate			Average inhibition rate	Accumulation	1- Accumulation	Accumulated inhibition rate
				First well	Second well	Third well				
900	6278	6376	6408	0.200051	0.187564	0.183486	0.190367	0.274635	0.809633	0.253290505
300	7692	9092	6394	0.0198777	0	0.18527	0.068383	0.0842678	1.74125	0.046161005
100	8960	7474	8190	0	0.047655	0	0.015885	0.015885	2.725365	0.005794856
33.33333	8530	8144	9682	0	0	0	0	0	3.725365	0
11.11111	7848	7848	7848	0	0	0	0	0	4.725365	0
Control	Cell	7848		Blank	0		Dilution	3	IC50	FALSE
Inhibition effect to HBsAg										
Concentration ($\times 10^4$ IU/ml)	First well	Second well	Third well	Inhibition rate			Average inhibition rate	Accumulation	1- Accumulation	Accumulated inhibition rate
				First well	Second well	Third well				
900	12364	12268	12274	0.036171	0.043655	0.043187	0.041004	0.140162	0.958996	0.12751773
300	11590	12708	13716	0.0965076	0.009355	0	0.035287	0.0991581	1.923709	0.0490186
100	12448	13468	13982	0.029623	0	0	0.009874	0.063871	2.913834	0.02144964
33.33333	12616	11346	12444	0.016526	0.115529	0.029935	0.053996	0.0539965	3.859838	0.013796309
11.11111	12828	12828	12828	0	0	0	0	0	4.859838	0
Control	Cell	12828		Blank	0		Dilution	3	IC50	FALSE

What is claimed is:

1. A recombinant super-compound interferon (rSIFN-co) with changed 3-dimensional structure and improved efficacy which can inhibit the DNA duplication and secretion of HBsAg and HBeAg of HBV.
2. The interferon of claim 1, wherein the 3-dimensional change was the result of changes of its production techniques, and efficacy gains not seen in interferon described in U.S. Patent Nos. 4,695,623 and 4,897,471.
3. A super-compound interferon of claim 1 or claim 2, wherein it has its unique secondary and tertiary structure which elicit its special efficacies.
4. A super-compound interferon of claim 1 or claim 2, produced by a highly efficient express system which is constructed with a special promoter.
5. The super-compound interferon of claim 4, wherein the promoter is P_{BAD}.
6. The super-compound interferon of claim 4, wherein its gene is artificially synthesized cDNA, adjusted according to codon preference of *E. Coli*.
7. A process for production of recombinant super-compound interferon recited in claim 1 or 2.
8. The process for production of claim 7, comprising extraction of super-compound interferon from fermentation broth, collection of inclusion body, denaturation and renaturation of the harvested protein.
9. The process of claim 7, wherein the process maintains the high efficacy even when the super-compound interferon is used with an agent and in a particular concentration.

10. The process of claim 7, comprising separation and purification of the super-compound interferon.
- 5 11. The process of claim 7, comprising lyophilization of purified super-compound interferon.
12. The process of claim 7, comprising production of liquid injection of super-compound interferon.
- 10 13. Uses of super-compound interferon in preparing medicines for inhibition of HBV-DNA, HBsAg and HBeAg, wherein the virus diseases comprising hepatitis A, hepatitis B, hepatitis C, other types of hepatitis, infections of viruses such as: Epstein-Barr virus, HIV, herpes viruses
15 (Epstein-Barr virus, Cytomegalovirus, herpes simplex viruses), papovaviruses, poxviruses, picornaviruses, adenoviruses, rihnoviruses, human T cell leukaemia viruses I, or human T cell leukaemia viruses II.
- 20 14. Uses of claim 1 and 2, wherein the super-compound interferon selected for interferon is α , β , γ such as, IFN-1a, IFN-2b or other mutants.
- 25 15. Uses of claim 13, wherein super-compound interferon was administered via oral, vein injection, muscle injection, subcutaneous injection, nasal, or mucosal administration.
- 30 16. Uses of claim 13, wherein super-compound interferon was administered following the protocol as follows: injection 9 μ g or 15 μ g per day, 3 times a week, total 24 weeks.