

## HIV Biotherapy and Natural Chemotherapeutic Agents

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### Abstract

Due to the limitation of present HIV/AIDS chemotherapies (incurable for HIV infected patients), new types of anti-HIV agents or clinical therapeutic strategies are desperately needed. Developing anti-HIV drugs of highly activity and penetrable into HIV-infected human cells and tissues is indispensable. HIV biotherapy and natural chemotherapeutic agents are those types of therapeutics. This article addresses the topics of HIV biotherapy and natural chemotherapeutic drug developments—including antibody or interferon therapy, modern diagnosis, genomic editing, Traditional Chinese Medicine, drug developmental pipeline innovation and so on.

**Keywords:** HIV drug developments; HIV therapy; Natural drugs; Traditional Chinese medicine; Biotherapy; Antibody; Interferon; Cytokine; Immunotherapy; Genomic editing

### Background

Owing to incomplete knowledge towards HIV/AIDS pathogenesis and mortality [1], the present chemotherapeutics is incurable for HIV/AIDS patients [2-5]. Several HIV-induced pathogenesis characters and human mortality are the causalities of HIV/AIDS treatment failures. To attain the goal of therapeutic cure, new types of anti-HIV agents or clinical therapeutic strategies capable to HIV clearance from patients are much needed.

### Therapeutic Rules

To develop anti-HIV drugs of highly activity and penetrable to HIV-infected human tissues, some important therapeutic options have been purposed for curing HIV-infected patients. Although a variety of anti-HIV agents or drugs (approximately 20-30 drug worldwide utility) have been licensed for clinical utilities, most of them are synthetic chemicals. Usually speaking, the specificity and therapeutic index of synthetic HIV chemicals is lower comparing with other types of drugs, (such as natural chemical drugs or bio-therapeutic drugs) for most refractory disease categories [6-9]. If we continue on this course for drug developments, we may loss the opportunity to cure HIV-infected persons in the first hands. Biotherapy or natural chemotherapeutic agents ought to display these characters. This is a golden opportunity for stepping up biotherapy and natural agent researches for HIV/AIDS therapeutics.

### The Source of Scientific Innovations

In many clinical circumstances, therapeutic drugs, such as anticancer drugs or antibiotics can better manage cancer growth and microbial infections in intermediate or even high concentrations or dosages by natural chemical drugs. More important, these types of drugs are capable to kill microbial and leukemia and other diseases in tolerable concentrations and dosages. In present anti-HIV drug arsenals, some first-line antiviral drugs are too toxic for patients to tolerate them for long term of clinical utilities. May we hope that some higher therapeutic-indexed anti-HIV drugs, such as biotherapy or natural-borne chemical agents will be developed for clinical utilities in future? Next generations of anti-HIV drugs should be penetrable into infected human cells and eliminate latent HIV virus in infected patients [6-9]. Following explanations are suggested for future HIV/AIDS therapeutic improvements and disease cure.

### Biotherapeutics Under Investigations

#### Antibody strategies

It has long been a long-standing paradigm for utilities of HIV vaccines or antibodies against viral infection, proliferation, viral-induced pathological progresses and human mortality. Again, human's antibodies against HIV have therapeutic efficacy and can be used in HIV treatments.

There are some flaws in antibody-based therapy (ABT) currently. Firstly, current antibodies are commonly homogeneous. However, a lot of diseases, such as cancer, avian flu and HIV are characterized as heterogeneous and diversity in pathogen populations, which will lead to different pathogen proliferation and disease progressions [10,11]. Thus, a homogeneous antibody only neutralizes or eliminates small proportion of HIV virus (<30% viral population in individual patient) or cancer in clinical trials [10,11]. Homogeneous antibody even facilitates the productions of resistant virus strains in infectious patients. So it is possible that some antibody cocktail could be used according to HIV genetic background in every HIV infected patients. By using antibody combination strategies, can we improve therapeutic efficacy of HIV/AIDS antibody treatments?

As a part of biotherapies, highly effective and safe viral vaccines are always the dream of majority virologists because many successful paradigms were available for two hundred years. One possible final solution of curing HIV/AIDS might depend on employing effective HIV vaccines [12-18].

#### Host defensive systems

For fully clearance of HIV viruses from patient's bodies, different types of biotherapies are proposed to be an ultimate solution for cure HIV/AIDS patient. Modulations of human defensive mechanisms and immune protective systems are the keys. The commonest and easiest

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way in future might be via HIV biotherapies including many attempts outside antigen-antibody system.

It has been long discovered that host (human) cells have their own defensive systems outside of antigen-antibody system. If we further study these systems, may we learn the underlying mechanisms of host defensive actions against deadly viruses and well manipulate them into good therapeutic paradigms (Table 1).

### Drug combination in new ways

Previously, we successfully combined chemical agents of different mechanisms (HAART) in HIV/AIDS treatments, which extended AIDS patient's survivals greatly. May we further suggest that combination of chemical agents with biotherapies might achieve more successes? May this strategy enable us to realize our dreams [2-5]. However it needs overall understandings of HIV infectivity, AIDS patients' pathogenic processes and human mortality.

## Natural Chemotherapeutic Agent Developments and Clinical Applications

Long before, it was discovered that natural chemotherapeutic drugs are higher efficacious and less toxic in disease control and therapeutics [19-27]. After this discovery, growing attentions have been focused on this drug development chain worldwide. Yet, these efforts still like finding needles from hay-stakes. New initiatives are proposed—including revisit drug development from ancient wisdom, especially from Traditional Chinese Medicine (TCM) [16-27].

### Major characteristics of natural chemotherapeutic agents

Differences between synthetic drugs and natural chemotherapeutic drugs, natural chemotherapeutic drugs are generally higher therapeutic efficacy—an aspects of higher therapeutic index. Analyzing from previously licensed drugs, the highest therapeutic indexed drugs often come from natural resources. For example, the most effective antibiotics (penicillin, streptomycin or cephalosporin) are natural products. They are much better than a series of synthetic agents (such as sulphonamide). These examples range from cancer treatment to viral epidemic control [6,9]. Figure 1 represent general outlook of natural drug discovery and developments.

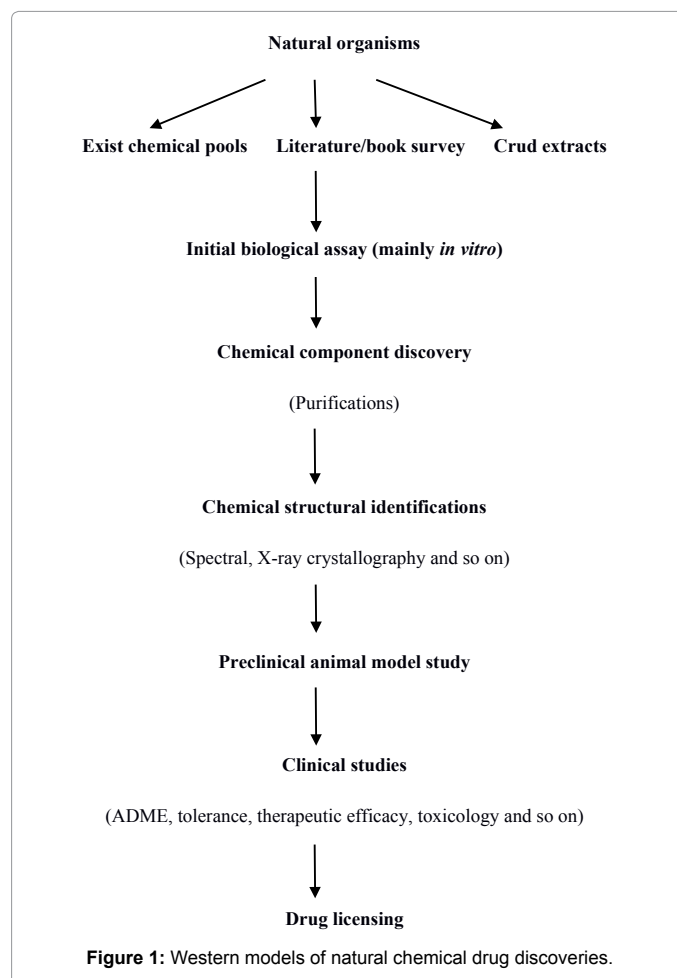
## Traditional Chinese Medicine As A Major Therapeutic Alternative

### Historic overview

China has a long history and reputations of the effective treatments for cold symptoms in large-scale human population (similar to viral infections like seasonal flu, avian flu and Ebola infections) endemic by TCM, which probably makes China the most populated country in the world. It has been repeated for viral epidemic control since the era of Zhong-Jin Zhang (AD150-219) in China [28].

Methods	Mechanism of action	References
Immunotherapy	Human defensive mechanisms	10
Antibodies	Virus binding and clearance	11
siRNA or other	Host cell defensive systems	14-15
Therapeutic vaccines	Human immune systems	16-18
Cytokines or interleukin	Cell defensive systems	19
Interferon	Virus infected cells	20
Exogenous DNA	Infected DNA	21
Recombinases	Penetrated viral segments in human genomes	22
Nucleases	Genomic editing	23

Table 1: Potential biological therapeutic options for HIV/AIDS treatments.



The biggest advantage of TCM over western medicine is higher percentage of cure rates in chronic diseases. As a result, systematic study of TCM for HIV/AIDS has a great potential.

### Therapeutic modality of TCM in HIV/AIDS treatments

Accordingly, virus-infected fever can be caused by patient's deficiency in "Yang" 陽—inner energy. TCM tries to combat these virus-induced disease symptoms by strengthening, modulating and offsetting damaged activities of human organ's "Yang" by formulated herbal medicines and large chemical component admixtures.

Since we guess that AIDS episodes are somewhat like deficiency in "Yang", people in western therapeutic theory may immediately think that "Yang promotion drugs/herbs can treat HIV/AIDS patients. However, this theory seems too simple to be performed in real clinical occasion. The drawback of this theory is that people are widely different between "Yang" (50%) and "Yin" (50%). Yang and Yin are opposite in clinical symptoms. Among all "Yang" and "Yin" symptom patients, 4 to 5 specificities can be categorized; including [阴阳 (yin/yang), 温寒(warmth/cold), 表里(superficial/inner condition), 虚(surreal/real)]. According to TCM philosophy, one or two fixed soups/herbal formulae could be universally utilized. You must adapt to TCM in such researches. Further work and clinical investigations are much needed. We only give several herbal formulae passed down from famous ancient TCM books [28-30].

### Drug prescriptions and common therapeutic formula in TCM

Different ways of drug combinations for infected patients are at

TCM doctor's disposal. Several formulated soups for cold symptoms (like viral acute infective stages) and high fever (commonly occurred in every deadly virus infections—similarity to avian flu symptoms) were applied by master Zhang, including “Gui-Zhi Soup”, “Ma-Huang Soup”, “Da-Qing-Long Soup” and “Ge-Geng Soup” [28]. These cheap medical herbs can be available all the times without any specific preparations. Historically, this theory has been successively controlling a great numbers of virus-infected endemics throughout the long history of China over 2,000 years [28]. We suggest that this type of treatment could be used in Ebola, HIV/AIDS epidemic control and virus clearance. More recently, Yin-Qiao-San was used in viral treatments in groups for expelling exogenous wind-heat symptoms. So was Jing-Fang-Bai-Du-San for expelling exogenous wind-cold symptoms. The utilities of Ma-Xing-Shi-Gan-Tang were to remove toxic heat obstruction in the lungs of infected patients with 100% effectiveness in clinical circumstances and practice [19-27].

### Current paradigms

Previously, ingredients from microbial or plants are very expensive. Now, these ingredients are much cheaper owing to technical advancements [9]. In future, we shall still maintain our momentum on TCM clinical practices against deadly virus, such as avian flu or Ebola in China. This is an overwhelming paradigm and long-term Chinese medical policy countrywide. Many ancient books can be carefully studied and for drug developers [28-30]. Nobel laureate for physiology and medicine (You-You Tu, China) of 2015 is the best paradigm of new anti-infective drug developments. She and other Chinese scientists discovered (青蒿素, Qing-Hao-Su or artemisinin) from referring a series of ancient Chinese medical books.

Generally speaking, TCM therapies are drug cocktail suitable for harmful viral infectious control and cancer treatments [19-27]. That needs time and paradigm propagation worldwide (Figure 2).

### Other Factors Association with these Therapies

TCM treats patients according to their symptoms. Many pathogenic symptoms such as pulmonary obstructions or high fever

can all be eased by TCM. Many new extracted chemicals from microbial or plants have higher therapeutic index comparing with synthetic chemicals. Previously, ingredients from microbial or plants are very expensive. Now, these ingredients are much cheaper owing to technical advancements [9]. In future, we shall still maintain and promote these clinical practices globally. This is an overwhelming paradigm and long Chinese medical traditions.

### Conclusion

Natural chemotherapeutic agents are important arsenal for controlling a great number of refractory genetic diseases and outsider viral/microbial invasion/infections. In future, we must focus on the discovery of chemotherapeutic agents and developments on this basis [31]. Some novel HIV therapeutic options such as biotherapies and natural chemotherapeutic agents have been under experimental investigations. With all these commitments, we feel safer than ever before. Look forward to the complete managements of HIV/AIDS.

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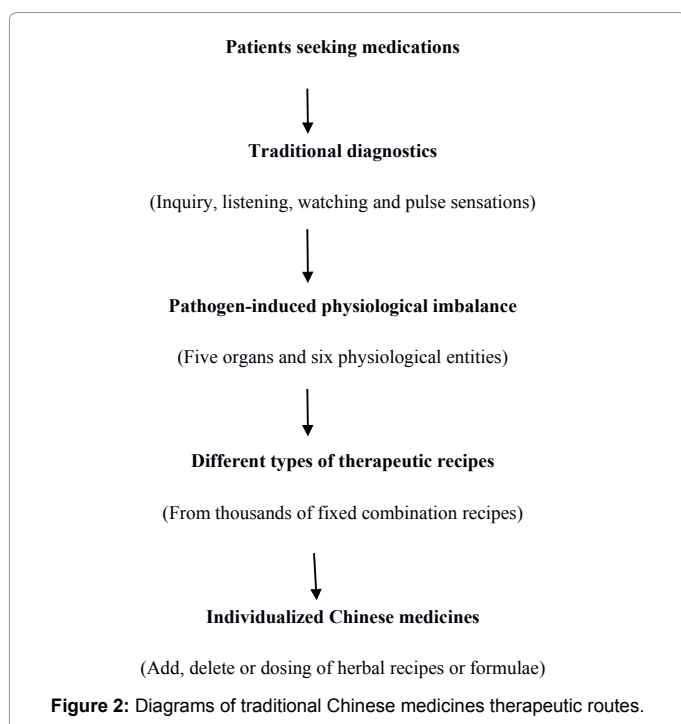


Figure 2: Diagrams of traditional Chinese medicines therapeutic routes.

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