Nanomedicine & Nanotechnology

Frazer RA, J Nanomedic Nanotechnol 2012, 3:1
http://dx.doi.org/10.4172/2157-7439.1000127

Review Article Open Access

# Use of Silver Nanoparticles in HIV Treatment Protocols: A Research Proposal

**Ricardo A. Frazer**

*Atlanta Metropolitan State College, 1630 Metropolitan Parkway, SW. Atlanta, GA, USA*

## Abstract

Current emphasis on elimination of the HIV/AIDS epidemic challenges researchers to assess the efficacy of alternative treatment modalities. Previous studies have been conducted using different silver preparations such as silver nitrate ($AgNO_3$) and silver oxide hydrosol ($Ag_40_4$) to treat HIV/AIDS patients. These studies did not use nanoparticles and used small sample sizes. Nanoparticle preparations hold particular promise because of their ability to enhance surface coverage. The present investigation is designed to test the efficacy of silver nanoparticle preparations using a pretest- posttest methodology. This research proposal is intended to increase awareness of a complimentary approach to HIV treatment and to stimulate future silver nanoparticle research.

**Keywords:** Silver nanoparticles; Oligodynamic silver; Silver oxide hydrosol; Acquired Immune Deficiency; Syndrome (AIDS); Complimentary Medicine

## Introduction

A number of medical researchers and practitioners have called for new drugs to combat HIV, because the replication process of the HIV virus results in numerous mutations, which can make the virus resistant to antiretroviral drugs [1,2]. Research suggests that oligodynamic silver ($Ag^+$) may be a viable complimentary treatment for the HIV virus, since silver has antimicrobial properties that selectively targets and kills rapidly proliferating single celled organisms such as bacterial, viral, fungi, protozoa and other pathogens, while normal tissues remain unaffected [3].

The toxicity of silver particles against a wide range of bacteria, viruses, fungi and other microbes has received a considerable amount of scientific investigation. The collective authoritative medical literature documents the efficacy of silver particles against over 24 viruses [3]. The list of viruses exhibiting silver cytotoxicity includes HIV [4-10]. Empirical investigation suggests that silver is an effective antiviral agent that may be useful in treatment and management of HIV/AIDS and other major diseases such as hepatitis B and hepatitis C, however additional human trials are sorely needed.

Researchers have demonstrated effects of silver nanoparticles in disturbing the replication of HIV viruses, *in vitro* [11]. Elechiguerra et al. [11] used electron microscopic images to observe interactions of silver nanoparticles with HIV-1. The exterior of the HIV virus was thought to be composed of a lipid membrane interspersed with protruding glycoprotein (gp) knobs. The main function of gp120 knobs is to bind with CD4 receptor sites on host cells. The mechanism by which HIV infects host cells is not fully understood. However, two steps in the process are broadly accepted. One step involves the binding of gp120 to the CD4 receptor sites on the host cell. In step two, a change is induced in gp120, resulting in exposure of new binding sites for co-receptor binding [11].

The chemical properties of nanoparticles depends on their interactions with capping agent molecules, since the surface chemistry of nanoparticles can modify their interactions with external systems [12]. Three types of nanoparticle preparations, each providing a different surface chemistry, were used in this study: foamy carbon, poly (N-vinyl-2-pyrrolidone), and bovine serum album.

All three capping agents exhibited inhibitory effects on viral replication. The toxicity of each preparation was determined [13,14,15]. Differences in HIV inhibition were explained in terms of the capping agents. The foamy carbon appeared to have a greater inhibitory effect on viral replication. However, this preparation exhibited greater cell toxicity [11].

Silver particles in each preparation exhibited a tendency to bind with to the 120 glycoprotein knobs, effectively blocking the binding with host cells. This research demonstrated a dose-dependent and a size-dependent interaction of silver nanoparticles with HIV. Elechiguerra et al. [11] concluded that silver nanoparticles in the range of 1-10 nanometers attached to the HIV virus effectively inhibiting the virus from binding to host cells [11].

In another *in vitro* study, testing the effects of silver nanoparticle cytotoxicity on HIV, researchers questioned the stability of nanoparticles for use in therapeutic applications. Previous research has demonstrated that silver particles tended to aggregate and settle rather than remain dispersed and suspended in solution [16]. These researchers employed human serum albumin (HSA) as a carrier solution for the silver. Anti-viral inhibition was measured using an ELISA method developed by Eberle and Seibi [17]. Researchers found that the nanoparticles buffered in HAS (hepes solution) caused the predicted anti-retroviral effects on HIV, yet revealed no spectral change. They found dose and size-dependent anti-retroviral activities for silver nanoparticles. These researchers concluded that silver nanoparticles fabricated in Hepes buffer solution will exhibit cytoprotective activities towards HIV infected cells [18].

One researcher has reported using silver oxide to eliminate the HIV virus in mice [19]. Antelman reported success in destroying the

***Corresponding author:** Ricardo A. Frazer, Atlanta Metropolitan State College, 1630 Metropolitan Parkway, SW. Atlanta, GA. 30310, Tel: 404-756-4707; E-mail: rfrazer@atlm.edu

**Received** December 07, 2011; **Accepted** December 27, 2011; **Published** December 29, 2011

**Citation:** Frazer RA (2012) Use of Silver Nanoparticles in HIV Treatment Protocols: A Research Proposal. J Nanomedic Nanotechnol 2:127. doi:10.4172/2157-7439.1000127

**Copyright:** © 2012 Frazer RA. This is an open-access article distributed under the terms of the Creative Commons Attribution License, which permits unrestricted use, distribution, and reproduction in any medium, provided the original author and source are credited.

virus in C57BL mice with a single intravenous injection. More research is needed to design to investigate the efficacy of silver oxide in the treatment of HIV-positive mice.

Clinical investigations of silver preparations in HIV treatment protocols have begun. One silver product in use is mild silver protein. In an *in vivo* investigation of mild silver protein, researchers used various concentrations of silver in the treatment of three patients with AIDS [5]. The subjects were treated with oral and intravenous administration of colloidal silver. Oral administration was started approximately one month prior to intravenous administrations. Subjects received progressively increasing concentrations of orally administered silver for 30-60 days. Patients were started on concentrations of 40 ppm and advanced to 400 ppm. Followed by 120 mL intravenous infusions of silver protein, at concentrations ranging from 40, to1500 parts per million. Oral administrations of silver were continued throughout the test period. All subjects experienced a significant drop in HIV viral loads and substantial improvement in their clinical condition. One patient's viral load dropped from 750,000 copies/mL to 39,00 copies/mL; another patients viral load dropped from 13,752 copies/mL to 2215 copies/mL. Viral load data was not obtained for the third patient, who ended treatment when his energy returned and he felt better. All three patients discontinued treatment when they felt better and able to return to their normal daily activities.

A negative side-effect was observed in the study. The three patients each experienced Jarisch-Herxheimer-like reactions. Administrations of silver continued but were moderated based on the severity of the reactions. Reactions decreased with repeated infusions and all three subjects recovered from the ill effects. The data are fragmented and incomplete as a result of early subject departures, however the results were not considered to be due to chance. Whether patients experience true Jarisch-Herxheimer reactions or inflammatory/toxic effects of the silver was not determined. The researchers concluded that intravenous infusions of mild silver protein up to 400 parts per million (ppm) appeared to be a safe and effective treatment agent for HIV-positive patients.

Nine terminally ill patients with AIDS related wasting and candidiasis were each treated with a single infusion of tetrasil tetroxide ($Ag_4O_4$), in another investigation with human subjects [4]. All subjects were removed from AZT therapy two weeks prior to inoculation with silver oxide hydrosol. These patients were all considered to be in moderate to poor condition. Body temperature and fatigue were also measured shortly after the silver oxide administration, since immune system improvements were viewed as important indications of treatment efficacy. The silver oxide hydrosol was administered at 40 ppm of blood volume. Pre and post CBC, CD4, body temperature and CD8 tests were conducted as well as overall clinical evaluation of general condition. All of the candidiasis patients showed a dramatic increase in white blood cell count (WBC). Two of the four patients with wasting syndrome showed improved WBS counts. Eight of the nine patients showed an increase in their white blood cell count from 10 - 350 percent. One of the nine patients did not show WBC improvement, but did show an increase in body temperature, which is suggestive of a positive immune response. One patient experience enlargement of the liver (hepatomegaly). However, there was no interference with liver function in any patient. Results varied for the individual patients, but overall, use of silver oxide showed excellent promise in the treatment of HIV-positive individuals. Silver oxide was thought to effect HIV treatment in the following way. Covalent binding with the virus and release of electrical energy through an oxidation reduction process. The oxidation process was considered to be necessary for the destruction of the virus. Tetrasilver tetroxide ($Ag_4O_4$), an electron-jumping compound, was thought to bind with the virus and electrocute it.

Only two published studies using silver as a treatment agent with HIV-positive patients were found. These studies suggest that human subjects can be safely and effectively treated with silver particles.

### Colloidal silver and particle size

Nanotechnology is at the cutting edge among today's scientific and technological advances. Nanotechnology has allowed scientist to engineer the properties of materials by controlling characteristics such as particle size. Silver nanoparticles have received considerable attention in medicine because of their ability to enhance surface coverage, with reduced toxicity considerations. For example, particles that have been dispersed into sizes below 10 microns will yield greater coverage over the surface area of cells, than particles above 10 microns in size. The nanoparticle also has an enhanced ability to react with its environment due to its high surface area. Particle surface area is the single most important property of colloids. Surface area increases as the concentration of metal particles increases. Surface area also increases as the particle size decreases. The higher the particle surface area, the more effective the colloid.

Ultrasound is one method used to achieve liquids composed of nano-size particles. Ultrasonic processors are used to reduce material slurries, dispersions and emulsions into nano-size particles. The ultrasound method uses cavitation forces to reduce particle size. Sonicating liquids at high- frequency or low intensity can cause cavitation. Cavitation is the formation, growth, and implosive collapse of bubbles in a liquid. While there are a number of methods such as rotor stator mixers, piston homogenizers, gear pumps, beat mills, colloid mills and ball mills, ultrasound is an efficient, well-established method for producing nano-size dispersions and emulsions [20].

## History of Silver Use

Silver is nontoxic to humans if properly used and it has a long history of medical and public health use dating back 6000 years. There are reports of silvers use in treating wounds by the ancient Egyptians and Macedonians [21]. The Druids lined their drinking bottles with silver and the ancient Greeks ate from silver utensils [21]. Silver has been used to purify water and to treat infections. It has also been used to sterilize surgical equipment and as plates in the surgical repair of bones [21]. Silver has been used to treat hundreds of ailments including syphilis, eczema, pneumonia, turberculosis, pleurisy, gonorrhea, leg ulcers and impetigo, from around 1893 until antibiotics came into common use [21]. Silver is classified as a multivalent metallic oxide rather than a heavy metal.

### Antimicrobial effects of silver

The antimicrobial efficacy of silver spans viral, bacterial, and fungal domains. Cytotoxic effects of silver on bacteria has been demonstrated for a wide range of bacterial microbes. The mechanisms by which these actions occur has not been determined, but a picture is developing. For example, Feng et al. [22] designed a study to determine the mechanism of the anti-bacteriological effects of silver [22]. A group of researchers had previously demonstrated synergistic effects of silver and hydrogen peroxide together on the viability of Escherichia coli k-12 [23]. Feng et al [22] designed a study to investigate the anti-bacterial effects of silver

alone. Two strains of bacterial were used in their study, gram-negative Escherichia coli and gram-positive Staphylococcus. For this study, 10 ug/mL of $AgNO_3$ was added to cultures of the two microbes. The researchers conducted x-ray microanalysis and electron microscopy and found that significant morphological changes occurred in the free state of DNA. They found that concentrations of silver granules appeared in the cytoplasm, around the cell wall, and in the DNA molecules. The observed changes suggested two mechanisms for silver's action. Proteins produced by the bacteria to protect the cells, DNA molecules fail, the cytoplasm membrane detaches, and electron dense silver ions cause the DNA to condense an action that causes DNA to loose its replication abilities. In turn, silver ions combined with thiol groups (in protein) which induce inactivation and deposition of bacterial protein, leading to death of the bacteria. In short, silver particles cause the DNA molecules to condensed and loose the ability to replicate. The loss of replication abilities was confirmed in the investigation [22].

Recognizing that colloidal silver is effective in treating microbes *in vitro*, a group of researchers designed a study to test the antibacterial actions of silver nanoparticles and $Ag^+$ ions, on *E. coli*. [24]. Two-dimensional electrophoresis and protein identification by mass spectrometry were the two approaches to proteomic analysis conducted. Parallel analyses with solutions of $Ag^+$ ions and Ag nanoparticles were conducted. The average diameter of the nanoparticles was 9.3 nanometers.

Eight envelope protein expressions profiles were stimulated in nanoparticle silver treated *E. coli* cells. OmpA, OmpC, OmpF, OppA, MetQ, are periplasmic components that guard against entry of foreign substances into the cell. S6, IbpA, and IbpB are proteins that function against stress induced protein denaturation. The researchers reasoned that translocation of proteins is mediated by preprotein translocase and requires ATP and protein motive force. Nanosilver was thought to dissipate membrane stability and de-energize the bacteria, culminating in loss of cell viability. Silver nanoparticles less than 10 nm in size penetrated the membrane. The antibacterial effects of nanosilver were similar to those of $Ag^+$ ions in that both had similar membrane dissipation actions and both were blocked by thiol containing agents. However, the effects of nanosilver are on the nanomolar levels, while the effects of $Ag^+$ are on the micromolar levels. Silver nanoparticles appeared to be significantly more efficient in mediating their antimicrobial activities than the Ag ions.

Researchers have also investigated the antifungal properties of silver [25]. Several species of candida albicans and one species of Torulopsis were treated with electrically generated metallic ions. Free ions of silver were studied (silver nitrate, silver sulfadiazine) as well as electrochemically generated silver complexes. A variety of metallic ions (silver, copper, zinc, titanium) were used in the study, however silver was the most reactive. The data showed that while all silver produced cytotoxic effects against yeast, the electrically generated silver ions were more effective than the silver sulfadiazine or silver nitrate.

The cytotoxic effects of silver on a large number of microbes have been established, *in vitro*. What is lacking is a clear understanding of the mechanisms by which these effects occur. Also lacking is an adequate testing of silver's efficacy in treating HIV-positive humans and knowledge regarding the full range of nanosilver activity in the treatment of individuals with HIV. Evidence does not suggest that silver nanoparticles cure HIV. Instead, existing data suggests that silver nanoparticles may serve as mid-range treatment in the effort to manage the disruption caused by HIV and other pathogens, since silver kills off HIV and other immune suppressing microbes without harming health cells. Silver acts as a catalyst for enzyme reactions in single-celled organisms without entering into chemical reactions with body tissue [21]. Clote [21] believes that silver cripples the oxygen-metabolising enzyme of one-celled organisms, thereby effectively suffocating disease causing pathogens [21].

### Toxicity

Reports on toxic effects of silver on the human body are mixed. One researcher indicated possible Herxheimer-type effects with repeated 120 mL infusions of silver protein above 400 ppm [5]. Other medical practitioners have found that long-term use of silver deposits metallic silver under the skin, causing a permanent affliction known as argyria, which is carcinogenic. Medical practitioners report that when silver administrations are kept within specified limits, and liver function is monitored, silver is a safe, effective anti-microbial agent which appears to decrease HIV viral load and improve immune function in AIDS patients [5,26].

The key to silver toxicity is particle size [26]. When silver nanoparticles are used, toxicity problems are averted. The diameter of the capillary lumen is 4-9 microns, as such the body has no problem excreting silver particles:

That is why there has not been a single case of Argyria from a properly manufactured modern day colloidal sliver product. The cases of Argyria reported in the 1920's and 1930's resulted because the technology of the day was unable to produce a colloidal silver product with a small enough particle size [26].

### The present Assessment

Previous *in vivo* studies have been conducted using different forms of $Ag^+$ ions such as silver nitrate ($AgNO_3$) and silver oxide hydrosol ($Ag_40_4$). These investigations did not employ nanosilver particles and used only a very small number of patients. The present study is designed to test the efficacy of silver hydrosol nanoparticles in treating HIV/AIDS patients. Participants will be excluded from this assessment if they have respiratory problems, are taking statins or cumidin, have karposis sarcoma, have an aneurism, liver disease, a cardiovascular event, a stroke, co-morbidity, pregnancy, or white cell titer.

## Methods

The pretest-posttest t-test quasi experimental design is selected for the current investigation. A low-dose (1200 ppm) and a high-dose (2500 ppm) treatment condition will be employed with 35 subjects in each group. Both groups will receive one intravenous infusion of picoscalar oligodynamic silver hydrosol administered once a week. Blood samples will be taken at the first intraveneous administration, the last administration, three months later and six months after the last intravenous administration. Blood sample assessments will be conducted for the four dependent measures used in this study: HIV viral loads, CD4 levels, T-cell counts and white blood cell counts. Other data such as body temperature, fatigue levels and standard clinical diagnostics will be collected for general appraisals of patient health and treatment efficacy. However, this general data will not be included in the main statistical analysis so that statistical power will be maintained. Fatigue will be measured for each individual before and after the silver treatment protocol using a fatigue scale developed by Chalder et al. [27]. Measures of perceived self-efficacy will be selected and administered to each individual prior to treatment. Research and theory suggests that

self-efficacy is an important factor in the adoption and maintenance of health behaviors [28].

## Discussion

It has been estimated that acquired immune deficiency syndrome (AIDS) has killed more than 25 million people since it was first recognized in 1981 [29]. Globally there are approximately 33.3 million people currently living with the human immunodeficiency virus as of 2009 [29].

There is currently no cure for AIDS or vaccines to prevent this disease. The treatment protocols generally considered to be most effective typically involve two or three different anti-retroviral drugs used in combination [29]. The use of antiretroviral drugs has reduced the morbidity and mortality associated with AIDS [30], however, a significant number of HIV infections have become resistant to antiretroviral treatment [1,2,31].

The use of alternative treatment approaches has been a widespread practice since the existence of HIV/AIDS was first reported by the Centers for Disease Control of Atlanta [32]. The cost and the politics of access to antiretroviral therapies, appears to have encouraged the use of these other treatment approaches. Stigma associated with HIV/AIDS and denial are factors which have obstructed testing for HIV and the use of antiretroviral drugs [33,34,35]. The effectiveness of alternative therapies has not been established, despite widespread use by people living with HIV/AIDS [36]. When used in conjunction with conventional antiretroviral therapies these approaches have at times been referred to as "complimentary" treatments.

Four different types of silver products are on the market for use in treating microbes. Colloidal silver products are colloidal suspensions of silver particles in water. Particles in silver colloid are typically 0.01 to 0.001 microns in diameter and carry a positive electrical charge [21]. The one type of colloidal silver is called electro-colloidal silver made either by electro-arc method in deionsed water or the low voltage electrolysis method in distilled water. Concentrations are usually between 3-5 ppm but sometimes as high as 100 ppm. Mild silver protein chemically binds microscopic particles of silver to a protein molecule and is usually found in concentrations between 50–500 ppm. Silver salts dissolve in water and usually contain elements other that silver. They can be made either chemically or electro-chemically. Concentrations range between 50 –500 ppm. Powdered silver is made when a pure silver wire is rapidly disintegrated by high voltage electricity. This dust is added to water or added to salves and creams for topical use. Silver products behave differently in the body and in laboratory tests. Dosage and quality vary considerably, and regulatory standards do not currently exist.

Silver hydrosol nanoparticles are presently used to treat HIV/AIDS patients who legally request alternative treatments of nanosilver from the Immune Recovery Foundation. Data will be collected from HIV/AIDS patients until approximately 70 patients are assessed. This information will be used for personal knowledge in treating patients with HIV/AIDS. A research of investigatory new drug (IND) form will be completed and filed.

Previous investigation with HIV/AIDS patients made use mild silver protein and silver oxide. Nano-silver is considered to be more efficient because a greater amount of cell surface area coverage is possible with nanoparticles. The results of this assessment will expand knowledge regarding the role of silver nanoparticles in HIV/AIDS treatment protocols.

### References

1. Bean P (2005) New drug targets for HIV. Clin Infect Dis 41: 96-100.
2. Bean P (2002) HIV genetic mutations causing resistance to the new drug T-20: recent findings. Am Clin Lab 21: 15-16.
3. Gordon E, Holtorf K (2007) A promising cure for URTI pandemics, including H5N1 and SARS: Has the final solution to the coming plagues been discovered? (Part II). Townsend Letter: The Examiner of Alternative Medicine.
4. Antelman MS (1997) Method of curing AIDS with tetrasilver tetroxide molecular crystal devices. United States Patent No. 5,676,977.
5. Dean W, Mitchell M, Lugo VW, South J (2001) Reduction of Viral Load in AIDS Patients with Intravenous Mild Silver Protein: Three Case Reports. Clinical Pract of Alternative Med 2: 48-53.
6. Oka H, Tomioka T, Tomita K, Nishino A, Ueda S (1994) Inactivation of enveloped viruses by a silver-thiosulfate complex. Met Based Drugs 1: 511.
7. Hussain S, Anner RM, Anner BM (1992) Cystine protects Na, K-ATPase and isolated human lymphocytes from silver toxicity. Biochem Biophys Res Commun 189: 1444-1449.
8. Making History: Curing HIV/AIDS with nanotechnology.
9. Fields CB, Burris PF (2000) Method for treating blood borne viral pathogens such as immunodeficiency virus. United States Patent No. 6,066,489.
10. Zhang ZY, Reardon IM, Hui JO, O'Connell KL, Poorman RA, et al. (1991) Zinc inhibition of renin and the protease from human immunodeficiency virus type 1. Biochemistry 30: 8717-8721.
11. Elechiguerra JL, Burt JL, Morones JR, Camacho-Bragado A, Gao X, et al. (2005) Interaction of silver nanoparticles with HIV-1. J Nanobiotechnology 3: 6.
12. Schmid GE (1994) Clusters and Colloids: From theory to applications. In Clusters and Colloids: From Theory to Applications. Weinheim 459-536.
13. Deng H, Liu R, Ellmeier W, Choe S, Unutmaz D, et al. (1996) Identification of a major co-receptor for primary isolates of HIV-1. Nature 381: 661-666.
14. Chackerian B, Long EM, Luciw PA, Overbaugh J (1997) Human immunodeficiency virus type 1 coreceptors participate in postentry stags in the virus replication cycle and function in simian immunodeficiency virus infection. J Virol 71: 3932- 3939.
15. Kaltenbach JP, Kaltenbach MH, Lyons WB (1958) Nigrosin as a dye for differentiating live and dead ascites cells. Exp Cell Res 15: 112-117.
16. Mafune F, Kohno J,Takeda Y, Kondow T (2000) Structure and Stability of Silver Nanoparticles in Aqueous Solution Produced by Laser Ablation. J Phys Chem B 104: 8333.
17. Eberle J, Seibi R (1992) A new method for measuring reverse transcriptase activity by ELISA. J Virol Methods 40: 347.
18. Sun RW, Chen R, Chung NP, Ho CM, Steve Lin CL, et al. (2005) Silver nanoparticles fabricated in Hepes buffer exhibit cytoprotective activities toward HIV-1 infected cells. Chem Comm 40: 5059-5061.
19. US Patent Claiming CURE for AIDS (2006) (USP # 5,336,499).
20. Hielscher T (2007) Ultrasonic production of nano-size dispersions and emulsions.
21. Cloete A (2007) All you need to know about Colloidal Silver.
22. Feng QL, Wu J, Chen GQ, Cui FZ, Kim TN, et al. (2000) A mechanistic study of the antibacterial effect of silver ions on Escherichia Coli and Staphylococcus aureus. J Biomed Mater Res 52: 662-668.
23. Liau SY, Read DC, Pugh WJ, Furr JR, Russell AD, et al. (1997) Interaction of silver-nitrate with readily identifiable groups – relationship to the antibacterial action of silver ions. Lett Appl Microbio 25: 279-283.
24. Lok CN, Ho C, Chen R, He QY, Yu WY, et al. (2006) Proteomic analysis of the mode of anti-bacterial action of silver nanoparticles. J Proteome Res 5: 916-924.
25. Berger TJ, Spadaro JA, Bierman R, Chapin SE, Becker RO (1976) Antifungal properties of electrically generated metallic ions. Antimicrob Agents Chemother 10: 856-860.
26. Farber P (1996) The Micro Silver bullet? CA: Professional Physicians Publishing & Health Services.

27. Chalder T, Berelowitz G, Pawlikowska T, Watts L, Wessely S, et al. (1993) Development of a fatigue scale. J Psychosom Res 37: 147-153.

28. Schwarzer R (1992) Self-efficacy in the adoption and maintenance of health behaviors: Theoretical approaches and a new model. In R.Schwarzer (Ed.), Washington, DC: Hemisphere 217-242.

29. Wikipedia:The Free Encyclopedia.

30. Palella F J, Delaney KM, Moorman AC, Loveless MO, Fuhrer J, et al. (1998) Declining morbidity and mortality among patients with advanced human immunodeficiency virus infection. N Engl J Med 338: 853–860.

31. Brenner BG, Turner D, Wainberg MA (2002) HIV-1 drug resistance: can we overcome? Expert Opin Biol Ther 2: 751-761.

32. Shanta TR (1991) AIDS-HIV: A perscription for survival. GA: International Publishing House.

33. Watson J (2006) Scientists, activists sue South Africa's AIDS 'denialists'. Nat Med 12: 6.

34. Baleta A (2003) South Africa's AIDS activists accuse government of murder. Lancet 361: 1105.

35. Cohen J (2000) South Africa's new enemy. Science 288: 2168-2170.

36. Mills E, Wu P, Ernst E (2005) Complementary therapies for the treatment of HIV: in search of the evidence. Int J STD AIDS 16: 395-403.

**Submit your next manuscript and get advantages of OMICS Group submissions**

**Unique features:**

- User friendly/feasible website-translation of your paper to 50 world's leading languages
- Audio Version of published paper
- Digital articles to share and explore

**Special features:**

- 200 Open Access Journals
- 15,000 editorial team
- 21 days rapid review process
- Quality and quick editorial, review and publication processing
- Indexing at PubMed (partial), Scopus, DOAJ, EBSCO, Index Copernicus and Google Scholar etc
- Sharing Option: Social Networking Enabled
- Authors, Reviewers and Editors rewarded with online Scientific Credits
- Better discount for your subsequent articles

Submit your manuscript at: www.editorialmanager.com/biochem