



A BIRD'S EYE PERSPECTIVE ON IMMUNOMODULATION THROUGH INCINERATED GOLD (*SWARNA BHASMA*) IN IMMUNOCOMPROMISED STATE OF HEALTH IN HIV

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ABSTRACT:

Introduction: HIV/AIDS, as the name itself suggests is a condition which manifest in an immunocompromised host who is very susceptible to opportunistic infections. Depletion in CD-4 T-cell count plays an integral part in the development of this immunocompromised state of health. **Materials and Methods:** Scientific literature search was done using Pubmed database and Google Scholar. Keywords used were *Swarna Bhasma*, HIV, AIDS, *Ayurved*, *Ayurveda* and Gold. Articles that have been published within the past 10 years were only reviewed. **Results:** Ayurveda does not believe in the concept of immunoboosters and immunosuppressants. Hence, immunomodulation or increasing *Vyadhikshamatwa* or Innate immunity in the patients is the primary line of treatment in *Ayurveda*. *Swarna Bhasma* or incinerated gold particles as well gold nanoparticles are proven immunomodulators in all age groups, from paediatrics to geriatrics. **Conclusion:** Original researches have evidences on the efficacy of gold preparations to increase CD-4 count in paediatric population as well as in animal studies. Hence, this therapeutic property of Gold can be very well explored in immunocompromised hosts of HIV-AIDS. Thus, this paper is an attempt to explore the therapeutic utility of Gold compounds of *Ayurveda* in immunomodulation in HIV/AIDS patients with impaired immunity.

Keywords: Communicable disease, HIV, Swarna, Gold, Ayurveda

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INTRODUCTION

Immunocompromised or Immunosuppressed state of health is a phase undergone by individuals either suffering from various diseases or conditions (AIDS, cancer, diabetes, malnutrition and certain genetic disorders) or undergoing medications or therapies (anticancer drugs, radiation therapy and stem cell or organ transplant). Having a weakened immune system makes it difficult for people who are immunocompromised to fight infections and other diseases.^[1] Depletion in CD-4 T-cell count plays an integral part in the development of this immunocompromised state of health. ^[2] The prevention of opportunistic infections occurring in immunosuppressed patients is primarily dealt with by improving the immune system of the affected individuals and especially CD-4 count especially when a person's CD4 count is below 200 cells/uL. There are a number of combination immunotherapies for these individuals to improve their immune system in modern medicine. Alternative medicine or traditional medicine is often resorted to by these patients even though there are no much strong evidences to prove the same. *Swarna Bhasma* as well as Gold nanoparticles/ salts can often act as a helping hand in this condition because of their immunomodulatory activity. Increasing *Vyadhikshamatwa* or Innate immunity in the

patients is the primary line of treatment in *Ayurveda*. *Swarna Bhasma* or incinerated gold particles as well gold nanoparticles/salts are proven immunomodulators in all age groups, from paediatrics to geriatrics. Thus, this paper is an attempt to explore the therapeutic utility of Gold compounds of *Ayurveda* in immunomodulation in individuals with immunocompromised state of health.

MATERIALS AND METHODS

Thorough scientific literature search was done using reliable search engines like PubMed, Google Scholar and Scopus. Keywords used were *Swarna Bhasma*, HIV, AIDS, *Ayurved*, *Ayurveda* and Gold. Articles that have been published within the past 10 years were only reviewed. The publications obtained were then segregated according to the type of study adopted and then thoroughly reviewed.

Results

Table 1: Analysis of published research on Immunomodulatory activity of Swarna Bhasma

Sl. No.	Author	Title	Study design	Outcome
1	P. Romagnoli et al.,1992	Gold-specific T Cells in Rheumatoid Arthritis Patients Treated with Gold	Clinical	The data obtained through the study suggest that gold can alter MHC-peptide complexes. This observation might explain the mechanism/s responsible for both the therapeutic and the toxic effects of gold.
2	U. Schneider et al.,2021	Intravenous gold-induced autologous serum injection therapy (Go ACT®) as a new treatment for seasonal pollen-based allergies	Clinical	Go ACT is safe, well tolerated and well accepted with good therapeutic outcome.
3	Rashmi Pareek et al.,2021	Evidence based study of effect of swarna yoga (gold formulations) in children: a systematic review	Systematic review	Review on clinical trials done till date suggest that gold formulations are safe and efficacious as a immunomodulator in children.
4	Menka Khoobchandani et al.,2020	New Approaches in Breast Cancer Therapy Through Green Nanotechnology and Nano-Ayurvedic Medicine – Pre-Clinical and Pilot Human Clinical Investigations	Clinical	Outcome of the study suggest that Swarna Bhasma can be safely used as a valuable adjuvant therapeutic agent along with chemotherapeutic agents.
5	Trupti Patil-Bhole et al., 2018	Assessment of bioavailability of gold bhasma in human participants e A pilot study	Clinical	Only traces are absorbed from single dose of Swarna Bhasma. Maximum bioavailability of Gold was observed from 30 mg sublingual dose with Cmax 0.983 mg/L at 2 h (Tmax).

6	Jyothy Kothanath Bhaskaran et al., 2021	Immunomodulatory activity of <i>Swarna Prashana</i> (oral administration of gold as electuary) in infants - A randomized controlled clinical trial	Clinical	<i>Swarna Prashana</i> did not interfere with normal growth of the infants. Swarna Bhasma also showed immunomodulatory activity and was tolerated by the infants with no adverse effects during the trial or follow-up period.
7	Branislava Janic et al.,2021	Therapeutic enhancement of radiation and immunomodulation by gold nanoparticles in triple negative breast cancer	Animal study	These results showing significant AuNP size-dependent RT enhancement and reveal additional underlying immunological mechanisms.
8	Daniel Beaudet et al.,2017	Comparative study on cellular entry of incinerated ancient gold particles (Swarna Bhasma) and chemically synthesized gold particles	In vitro (cell-line)	IAuPs were in vesicles, cytosol, or in the nucleus. Their nuclear accumulation likely occurred after nuclear envelope breakdown during cell division. Larger IAuPs entered cells via macropinocytosis, while smaller particles entered via clathrin-dependent receptor-mediated endocytosis.
9	Abdulrahman M Elbagory et al.,2019	The In Vitro Immunomodulatory Effects Of Gold Nanoparticles Synthesized From Hypoxis hemerocallidea Aqueous Extract And Hypoxoside On Macrophage And Natural Killer Cells	In vitro (cell line)	The four treatments (H. hemerocallidea extract, hypoxoside and their respective AuNPs can lower the pro-inflammatory cytokine levels in the macrophages cells, while only AuNPs produced from hypoxoside can reduce cytokine responses in NK cells.
10	Keisuke Hashimoto et	Immunomodulatory Effects of Therapeutic Gold	In vitro (cell line)	The immunomodulatory effects of GST may result from its capacity to inhibit

	al., 1992	Compounds		PKC activity. Human T cell proliferation and interleukin 2 production by Jurkat cells were inhibited by GST or AUR at pharmacologically relevant concentrations.
11	Snehasis Biswas et al., 2019	Physicochemical characterization of <i>Suvarna Bhasma</i> , its toxicity profiling in rat and behavioural assessment in zebrafish model	Analytical and animal study	XRD study revealed that all the peaks of <i>Suvarna Bhasma</i> match well with pure gold (face centred cube) with crystallites size 45 ± 2.8 nm. In zebrafish behavioural study, the motor parameters of <i>Suvarna Bhasma</i> treated fish showed normal behaviour analogous to the vehicle control group.
12	Kapil Thakur et al., 2017	Preparation and Characterization of Suvarna Bhasma Parada Marit	Analytical	The XRD study showed Suvarna Bhasma to be crystalline in nature and to contain more than 98% gold. The mean size of the gold crystallites was less than 10 microns, and the morphology was globular and irregular.
13	Prabhudas Nelaturi et al., 2020	Swarna Bindu Prashana—an Ancient Approach to Improve the Infant's Immunity	Review	The plausible mechanism of SBP in dendritic cells maturation and subsequent T cell activation has been described in this review. SBP is an immune booster for infants against any viral disease
14	Shuang Yue et al., 2020	Recent Advances of Gold Compounds in Anticancer Immunity	Review	The property of gold compounds is expected to combine with anticancer immunotherapy, such as immune checkpoint inhibitors, to develop new anticancer therapeutic strategies.
15	Pascaline N.	HIV therapeutic possibilities	Review	Gold-based compounds have shown

	Fonteh et al.,2010	of gold compounds		promising activity against a wide range of clinical conditions and microorganism infections including HIV-1. A typical example is auranofin which resulted in an elevated CD4 and T-cell count in an HIV patient being treated for psoriatic arthritis. In addition, reports exist on gold-based inhibitors of reverse transcriptase (RT), protease (PR) and viral entry of host cells.
16	Lev A. Dykman et al.,2020	Gold nanoparticles for preparation of antibodies and vaccines against infectious diseases	Review	Gold nanoparticles can be used as adjuvants to increase the effectiveness of vaccines by stimulating antigen-presenting cells and ensuring controlled antigen release. Studying the characteristics of the immune response obtained from the use of gold nanoparticles as a carrier and an adjuvant will permit the particles' potential for vaccine design to be increased.
17	Akshita Chauhan et al., 2021	Design and Encapsulation of Immunomodulators onto Gold Nanoparticles in Cancer Immunotherapy	Review	As gold is highly biocompatible, GNPs can be administered intravenously, which aids in increasing cancer cell permeability and retention time. As a result, GNPs are a useful vehicle for delivering antigens and adjuvants that support the immune system in killing tumor cells by facilitating or activating cytotoxic T lymphocytes.

DISCUSSION

Swarna Bhasma has been characterised using advanced analytical techniques in previous studies as composed of polycrystalline Gold with face cubic crystalline lattice at a percentage level of more than 90% along with the absence of any organic matter and mean particle size ranging from 2 to 4 micrometres.^{[3],[4]} The therapeutic potential of gold salt, namely Auranofin, as an add on treatment to ART has been proven effective and has indeed improved CD-4 count thus strengthening the immune system of the patients.(ClinicalTrials.gov identifier: NCT02961829).^[5] Application of gold nanoparticles has also been studied with respect to its capacity to improve immunity as well as suppress the virus multiplication but also target the viral entry area by attaching with gp120 (glycoprotein 120), and inhibit the binding with CD4 (Cluster of differentiation 4) T cells. ^[6] Chemically synthesized Gold nanoparticles are also studied for their effect on immune system in terms of their ability to cause significant changes to dendritic cells. Dendritic cells play a major role in both innate and acquired immune responses. Gold nanoparticles does not cause any phenotypic change to the dendritic cells. Shape of these particles influences the activation of these cells since they cause effect on the immune

system through different cytokine pathways.^[7]

There is a potential role played by TNF- α in the increased activation of the peripheral immune system. Gold nanoparticles caused a wide variety of inflammatory stimuli, in response to which large amounts of TNF- α was secreted.^[8] Moreover, internalization of these particles are observed causing significant modification in secretion of cytokines which might be the most probable cause for the perturbation of immunity.^[9] These particles would also prevent the stimulation of auto aggressive T cells through the modification of putative "autoimmune peptide-MHC complexes" and thus leading to the formation of Gold-specific T cells.^[10] All these studies and researches have made modern medicine also to look forward towards the application of gold in treatment of HIV/AIDS as an immunotherapeutic agent. ^[11] Hence, this therapeutic property of Gold can be very well explored in immunocompromised hosts of HIV-AIDS by incorporating *Swarna Bhasma* and other Ayurvedic gold formulations into HIV/AIDS treatment. Steps have been taken forward in this direction by Ayurvedic practitioners themselves, in Pune through the therapeutic application of a combination of drugs, which includes *Makaradhwaja* also, which is a gold preparation.^[12] Original researches have evidences on the efficacy of

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Ayurvedic gold preparations to increase CD-4 count in paediatric population as well as in animal studies.^[13] The biological safety of *Swarna Bhasma* from clinical point of view has been established which suggests the therapeutic application of the same in Paediatric population affected with HIV/AIDS as well.^[14] Increased bioavailability of Gold salts such as sodium theomolate (100% bioavailable) and Auranofin (20% bioavailable) can be attributed to the routes of administration and the chemical and physical composition of the drugs as well. In case of *Swarna Bhasma* sublingual route of administration showed maximum bioavailability.^[15] Lowest dose of Gold nanoparticles have showed significant increase in the synthesis of proinflammatory cytokines like IL-1, IL-2, IL-6 and TNF- α which are known to have an immune-stimulating effect.^[8] Trace level absorption may attribute for the safety and efficacy of *Swarna Bhasma*. Thus, all these evidences lead us to a postulation that this immunomodulatory activity of *Swarna Bhasma* can be very well implemented in the therapeutic strategy of HIV/AIDS.^[16]

CONCLUSION

The future prospects of treatment in purview of immunomodulation in communicable diseases lies safe in the hands of *Ayurveda*. *Swarna* is just a mere example of the same.

There are infinite number of formulations having such wonderful immunomodulatory property which can be very well adopted in treatment of such immunocompromised conditions in various communicable diseases.

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