



SWARNA BHASMA AND GOLD COMPOUNDS: AN INNOVATION OF PHARMACEUTICS FOR ILLUMINATION OF THERAPEUTICS

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ABSTRACT

Mankind, since its genesis i.e. chronological evolution to till date possesses strong desire to live long with continuum power and vigor. He upholds this aspiration by adopting measures in his diet, duties and drugs. Among drugs Gold constantly held supreme stratum on virtue of its therapeutic properties in every system of medicine. Mostly Swarna Bhasma is a functional dosage form in the Ayurvedic treatment along with few others. Whereas in conventional system of medicine several molecules of Gold are accomplished for management of various disorders.

The conversion of metallic Gold to medicinal gold (either Swarna Bhasma or Gold compounds; chemical entity of conventional system) is an exemplary example of promising potentials of Pharmaceutical branches of both system of medicines.

In this review paper an assortment of facts about clinical application of Swarna Bhasma and Gold compounds have been congregated from both system of medicine and supplemented with concurrent references of research papers. An analysis of essentials of Gold reveals its exclusivity in therapeutics as rejuvenator, immunomodulator and certain chronic disorders.

Keywords: Gold, Swarna Bhasma, Marana, Immunomodulator, Rheumatoid Arthritis

INTRODUCTION

Rasa Shastra, better known as Ayurvedic Pharmaceutics, deals with standard quality production of herbo-mineral formulations used in the healing practices of Ayurveda with ultimate objective of strengthening of health. Metallic formulations are unique to Ayurveda and as such it is said that,

“Mritāni lohāni rasi bhavanti, nighnanti yuktāni mahāmayansch.

Abhyāsa yogat dridha deh siddhim, kurvanti ruk janma jarā vināsanam”¹

It means that if metals/minerals are properly incinerated/calcined in to fine powder form, on internal use they get absorbed and assimilated into the biological system like Adya Rasa dhātu: primary physiological fluids essential for survival of human. They get converted into targeted drug form and their proper use may eradicate all types of ailments and their prolonged use provides good strength and immunity power to the life with ultimate delayed ageing process.

The therapeutic indication of Swarna/Gold are common features of approximately all ancient classics viz Charak Samhita(1500 BC), Sushruta Samhita (1000 BC), Astang Hridaya (400 AD) in genral. Around forth century development of Rasa Shastra started and onwards Swarna have been addressed very categorically in text books of Rasa Shastra with master stroke of its pharmaceutics and therapeutics. Swarna considered superior among all metals and is kept under Sara loha group means essence or noble metal. It has been used in calcined form (Swarna Bhasma) in various ailments like tuberculosis, anemia, cough, debility, sterility, muscular dystrophy.² It is considered as best rejuvenator promotes longevity and prevents ageing.³

The time tested properties of Swarna Bhasma are being proved once again by modern researchers to withstand the ancient system of medicine on modern scientific

parameters. Various studies have been conducted in past few years to prove the healing and health promoting properties of gold. The effect of gold in the body is also being considered by modern science and they are using gold in various chemical forms in therapeutics as well as diagnostics. Although constituency, mode of action of Swarna Bhasma and gold compounds may be different but ultimate objectives of both medicinal form of gold is same i.e prevention and cure of diseases for better life.

GOLD IN TRADITIONAL SYSTEM OF MEDICINE AS SWARNA BHASMA

Form of Gold in Ancient era

In traditional system of medicine (mainly Indian and Chinese), gold was used either as Swarna Bhasma, Swarna Parpati, Swarna Patra or as red colloidal solution. In Ayurvedic bhasmas, the gold is used in the form of purified metallic fine powder (probably as nano-particles) or red colloidal solution where both are prepared by elaborate treatments including using herbal extracts and even with other metals.⁴

Pharmaceutical Procedures Employed in the Preparation

The pharmaceutical procedures of preparation of Swarna Bhasma are based on procurement of best quality of Swarna, its process of Shodhan (purification/potential) and Marana (incineration/calcinations) which are very specified in terms of procedure, equipment used, media (intermediary herbal juices, decoction), heating pattern and its frequency. This is worthy to quote here that all these parameters are solely depending on physico-chemical properties of raw material to be exposed for processes and desired chemical constituencies as bhasma which will act as medicine. Swarna Bhasma is prepared as per classical references indicated for Shodhan and Marana of Swarna.^{5,6,7}

Chemical Characterization

Swarna Bhasma prepared with media of mercury was shown to contain 92% gold by Atomic Absorption Spectroscopy. However, mercury was not detected in the sample. The XRD study was conducted. The diffraction peaks at $2\theta = 38.2^\circ, 44.4^\circ, 64.6^\circ$ and 77.6° are identical with those reported for the standard gold metal (Au_0) (JCPDS, USA). No other diffraction peaks were observed confirming that the drug Swarna Bhasma is composed of mainly gold nanoparticles.⁸

Particle size and Morphology

An image from the Transmission Electron Microscopic study shows the average particle size of Swarna Bhasma

to be 57 nm with globular morphology. The globular nature of Swarna Bhasma was confirmed by Atomic Force Microscopy.⁹

Pharmacological Properties of Swarna Bhasma

The therapeutic properties of Swarna Bhasma are depicted in Table 1. Some formulation of Ayurveda which consists of Swarna Bhasma as constituent is also shown in Table 2 with therapeutic indications.

Researches performed in recent past are quoted as under mentioned to substantiate the claim of Swarna Bhasma in Ayurvedic classics in pattern of reverse pharmacology.

Table 1: Therapeutic efficacy of Gold (Swarna bhasma) as described in Ayurvedic classics

S. No.	Name of Book	Dose	Indications*
1.	Rasa Ratna Samucchya	2 Ratti	Kshya, Agnimandya, Swasa, Kasa, Aruchi, Sangrahi har, Ojo dhatu vivardhana, Balakar, Pandu Roga har, Sarva Visha har.
2.	Rasa Prakash Sudhakar	½ Ratti	Saundarya Kanti vardhana, Tridoshaja Roga, Visha nashaka, Prevents ageing on using 20 years
3.	Ayurved Prakash	1 Yava- 8 Ratti	Vrishya, Balya, Rasayana, Brinhana, Netrya, Medha smriti pradam, Hradya, Ayushya, Kanti, Vagvishuddhi, Vish har, Kshaya, Unmadhar
4.	Rasa Tarangini	1/8- ¼ Ratti	Vrishya, Hradya, Netrya, Smriti prada, Medhya Rasayana, Punsavanopyggi, Vishhar, Kantikar, Varnya, Visama Jwarahar, Antra Shosha Kshayaghnam
5.	Rasamrit	1/8- ¼ Ratti	Vishaghna, Varnya, Medha smriti vardhana, Rasayana, Medhya, Yakshma Unmada prasamana, Sarva Doshaha

* Indications are presented here as per Ayurvedic terminology of different diseases which are very much similar to diseases of respiratory system, GIT, Immunoenhancers of the conventional medical system.

Table 2: Formulations in market containing Swarna bhasma

S. No.	Name of Drug	Disease	Dose (in mg)
1.	Brhat Vata Cintamani Rasa	Vatavyadhyadhikara (Diseases of nervine origin)	125
2.	Vasant Kusumakar Rasa	Prameha (Diabetes)	125-250
3.	Swasa Kasa Chintamani Rasa	Swasa, Kasa (Asthma, Cough)	250
4.	Purna Chandrodaya Rasa	Rasayana, Vajikarana (Immunomodulator, Aphrodisiac)	125- 250
5.	Brahmi Vati	Manoroga, Hrid daurbalya (Mental disorders, Heart diseases)	125-250
6.	Jayamangala Rasa	Jirna Jwara (Chronic fever)	250
7.	Kumarkalyana Rasa	Bala Rogadhikara (Paediatric diseases)	62.5
8.	Sutasekhara Rasa	Amlapitta Chikitsa (Acidity)	250
9.	Brhat Garbha Chintamani Rasa	Sutika Roga Chikitsa (Puerperal diseases)	250
10.	Suvarna Malini Vasant Rasa	Rajyakshma (Tuberculosis)	125

Free- radical Scavenging Activity

During planned experimental studies Swarna Bhasma has shown free radical scavenging activity. There are several proteins and enzymes present in our body that reduce the generation of reactive oxygen species (O_2^- , OH^- , H_2O_2 etc.) Two such key enzymes viz. Superoxide dismutase (SOD) and catalase were measured after oxidative insult with acetic acid in both Swarna Bhasma treated as well as control animals serum and/or liver homogenate. Swarna Bhasma enhanced activity of SOD (267% in case of serum SOD and 75.8% in case of liver homogenate, SOD activity compared to the respective controls) and catalase (80% compared to control haemolysate) which can be correlated with the improved pathophysiological conditions of the patients.¹⁰

Anti Cataleptic, Anti-anxiety and Anti-depressant Activity

Swarna Bhasma caused significant increase in punished drinking episodes in anxiometer and open arm entries and time in elevated plus maze and decrease in behavioral deficit. A decrease in immobility time in forced swimming test, normalization of shock- induced escape failure in learned helplessness test, and reduction of haloperidol induced catalepsy scores were also noted in treated animals.¹¹

Analgesic Activity

A calcined gold preparation, Ayurvedic Swarna Bhasma was investigated for analgesic effects in rats and mice using four types of noxious stimuli. The test drugs exhibited analgesic activity against chemical (acetic acid induced writhing), electrical (pododolorimeter), thermal (Eddy's hot plate and analgesimeter) and mechanical (tail clip) test. The analgesic effects of Swarna Bhasma could be partly blocked by pretreatment with naloxone (1-5 mg/kg, i.p.,--15 min). Involvement of opioidergic mechanism is suggested for the observed analgesic activity.¹²

Antioxidant/ restorative effects Against Global and Focal Models of Ischaemia

Enzymatic parameters (lipid peroxidase, reduced glutathione, catalase, glutathione reductase, glutathione-S-transferase, glutathione peroxidase, superoxide dismutase, and glucose-6-phosphate dehydrogenase) were employed to assess ischaemic brain damage and its modulation. Significant restoration of altered values to near normal levels by Ayurvedic Swarna Bhasma suggest potentials for gold preparations in cerebrovascular diseases.¹³

Augmentation of Non-specific Immunity

Male mice were administered with the incremental doses of the drug orally for 10 days. Parameters of study included body weight, organ weight, peritoneal exudate cell (PEC) counts and phagocytic activity of PEC. Swarna Bhasma significantly ($P < 0.001$) increased counts of peritoneal macrophages and stimulated phagocytic index of macrophages.¹⁴

Safety and efficacy

Gold containing Ayurvedic preparation, Swarna Vasant Malti, was given to 20 male persons in a dose of 100 mg twice a day for 40 days under supervision of Ayurvedic physicians. The total cumulative intake of 160 mg of gold at the rate of 4 mg per day in this form did not have any toxic effect on human body as evidenced by clinical examination, unaltered body weight, absence of urinary pathology and by 30 sensitive biochemical and enzymatic tests. The gold from this Ayurvedic preparation was found in plasma and erythrocytes, excreted partly in urine and was present in semen. This gold preparation seemed to increase sperm motility and prostatic activity.¹⁵

GOLD IN CONVENTIONAL SYSTEM OF MEDICINE

Gold is predominantly used for its immunomodulatory activity in present era although its uses in diagnostic tools are also reported.

Form of Gold Used in Modern Science

In the West, alchemists sought a form of gold that can be orally consumed as 'potable gold (gold trichloride, gold tribromide, gold thiomalate, gold thioglucose, complex organic salt of gold, auronofin, etc.) for a plethora of diseases. Western tradition, the gold was generally used in ionic form as pure salts like gold trichloride, gold bromides etc.¹⁶

Effect on Skin Condition (Pemphigus)

Concentrations of gold in skin achieved during systemic chrysotherapy inhibited prostaglandin synthesis *in vitro*, using a sheep vesicular gland dioxygenase system. Two human epidermal enzymes, acid phosphatase and tryptophanyl-tRNA synthetase, were also inhibited by gold *in vitro*. These findings suggest some possible mechanisms of gold action in pemphigus, such as interruption of the inflammatory cycle and inhibition of skin enzymes involved in blister formation.¹⁷

Effect of Gold Nanoparticles in B-chronic Lymphocytic Leukemia (BCLL)

B-Chronic Lymphocytic Leukemia (CLL) is an incurable disease predominantly characterized by apoptosis resistance. The induction of apoptosis with gold-AbVF was significantly higher than the CLL cells exposed to only AbVF or GNP. The gold-AbVF treated cells showed significant down regulation of anti-apoptotic proteins and exhibited PARP cleavage.¹⁸

Effect on Reproductive Function in Immature Female Albino Rats

Significant increase in ovarian and uterine weight Δ^5 - 3β hydroxysteroid dehydrogenase activity and elevation of serum estradiol level were observed following gold chloride (0.2 mg/kg body weight/day), s.c. administration in immature female albino rats. Histological study of ovary also showed Graafian follicle with ovum in rats proving stimulation of reproductive function.¹⁹

Effects on Testicular Steroidogenic and Gametogenic Functions

0.5 mg gold chloride treatment for 26 days caused a significant increase in plasma T ($p < 0.001$) along with stimulation of testicular Δ^5 - 3β -HSD (hydroxysteroid dehydrogenase) activity ($p < 0.001$) and 17β -HSD activity ($p < 0.001$). Gametogenic activity exhibited a significant increase in the number of step 7 spermatids (7Sd) ($p < 0.001$) at stage VII of seminiferous cycle when compared to control.²⁰

Effect on Substance P levels in Rheumatoid Arthritis

The effect of gold salt therapy on substance P immunoreactivity levels in plasma and synovial fluid was studied in 42 patients with rheumatoid arthritis. Decreased levels of synovial fluid substance P, although not statistically significant, were found in rheumatoid patients who were currently receiving gold therapy when compared to either those patients previously treated or to those who never received this therapy. In addition the researchers found that patients who received more than 1000 mg of gold salts had significantly lower levels of substance P in synovial fluid than those treated with lower doses. These results therefore, seem to support the hypothesis that gold salts appear to be slow-acting neurotoxic drugs that significantly decrease the intrasynovial concentrations of substance P, a well-known inflammatory neuropeptide, in arthritis patients.²¹

Effect of Colloidal Gold and Sodium Thiomalate in Treating Arthritis

Colloidal metallic gold (average particle size 27 nm) is a far more potent and effective anti-arthritis agent in rats than the sodium aurothiomalate (I) used to treat rheumatoid arthritis. The reported data show that Au⁰ administered subcutaneously (s.c.) suppressed development of three different forms of arthritis in rats. By contrast, s.c. aurothiomalate (1) at almost 10^3 times as gold dose was effective only against the arthritis induced with a mycobacterial adjuvant. This is the most inflammatory of these three forms of arthritis and characterised by active leukocytes generating reactive oxygen-derived species e.g. H₂O₂.²²

Effect on Antipermeability and Antiangiogenic Properties

Gold nanoparticles have unique anti-angiogenic property. Gold nanoparticles inactivate heparin binding growth factors by interacting through the heparin binding domain. Gold nanoparticles decrease permeability and inhibit angiogenesis *in vivo*. Gold nanoparticle is the first example of an inorganic compound that is anti-angiogenic in nature.²³

Effect on Modulation of the Immune Response

The effects of gold on immune responses was reviewed. Gold salts used therapeutically can be followed by a decline in serum immunoglobulin levels, and rheumatoid factor titers in rheumatoid arthritis; in pemphigus there is similarly a drop in anti-epithelial antibody titers. Gold inhibits stimulation of immunoglobulin-secreting cells. Gold inhibits the activation of the classical and alternate complement pathways. Gold compounds inhibit numerous cell-mediated immune responses to various mitogens and antigens. Inhibition may be due to the effect of gold on macrophages acting as helper cell in these reactions. Auranofin is a new oral compound which

seems to be particularly potent in its immuno-regulatory actions; it differs from other gold compounds in its pharmacokinetics, and in the nature of its ligand. Gold has also been reported to enhance certain immune reactions. The extent of the immuno-regulatory effects of gold *in vivo* is unknown, and the relation of these effects to its therapeutic actions remains to be clarified.²⁴

In one such research to study effect of gold on immune response, separate concurrent injection of organic gold compounds and antigen into mice resulted in immunoenhancement that could be measured by direct and indirect plaque-forming cells, rosette-forming cells, and serum antibody assays. Kinetics of the immune response showed variable effects through day 9 of the experiment. Studies with British anti-lewisite, a gold antagonist, showed that the gold must stay in the system 1 day to obtain immunoenhancement.²⁵

Application of Gold as Diagnostic tool

In fact nanoparticles of metal or metal sulphides, including nano-gold particles, are being considered to have great potential in various therapeutic and diagnostic applications in modern medical system.²⁶

Nano Gold in Cancer Detection: (anti EGFR)

Binding gold nanoparticles to a specific antibody (EGFR) for cancer cells could make cancer detection much easier. Gold nanoparticles stick to cancer cells and make them shine, and are very good at scattering and absorbing light. Many cancer cells have a protein, known as Epidermal Growth Factor Receptor (EGFR), all over their surface, while healthy cells typically do not express the protein as strongly. By conjugating, or binding, the gold nanoparticles to an antibody for EGFR, suitably named anti-EGFR, researchers were able to get the nanoparticles to attach themselves to the cancer cells.²⁷

Reported Gold Toxicity

It has been found that there are at least three forms of gold induced side effects namely painful neuropathies occasionally accompanied with insomnia and anxiety, peripheral neuropathy, and encephalopathy with symptoms like depression and delirium.²⁸

DISCUSSION

This is very true that application of Swarna Bhasma is time tested in Indian civilization with a praiseworthy therapeutic efficacy. Not only Swarna Bhasma but utensils of Gold were also in practice in ancient times with the objectives of prevention of disease, Swarna prashan was a highly admirable ritual in high society.

Now, it has been established that Swarna Bhasma is in range of nano particle size and remains mostly in form of mono atomic gold.²⁹

The success of preparing a genuine Ayurvedic bhasma depends on the technique of heat treatment (called as *putas*) to the homogeneous paste prepared by mortaring microfinned metal thoroughly mixed with appropriate plant juices. Normally a large number of calcination cycles are necessary and for each cycle the process of mortaring the microfinned metal and plant juice is to be freshly repeated. Therefore synthesis of these bhasmas is a complicated and tedious procedure and Ayurvedic experts prepared these bhasmas on certain SOP and GMP norms notified by dept of AYUSH for the same.³⁰

Recent researches proved that Ayurvedic pharmaceutical procedures are enough capable to convert raw materials of metallic origin into form of nano particles. A study at National Chemical Laboratory ascertains these facts on gold. A close comparison of method and material sustain the claims.³¹

This has been proved that nano structure of a material is changed material in every aspect from parent material. The discovery that nanoscale gold particles function as active and selective catalysts for a variety of important chemical reactions has provoked much research interest in recent years.³²⁻³⁷

Researchers have also reported the mode of action of metal nano particles in detail. Harvard Medical School researchers report in the Feb. 27 issue of Nature Chemical Biology that special forms of gold, platinum, and other classes of medicinal metals work by stripping bacteria and virus particles from the grasp of a key immune system protein.

MHC class II proteins are associated with autoimmune diseases. MHC class II proteins normally hold pieces of invading bacteria and virus on the surface of specialized antigen presentation cells. Presentation of these pieces alerts other specialized recognition cells of the immune system called lymphocytes, which starts the normal immune response. Usually this response is limited to harmful bacteria and viruses, but sometimes this process goes awry and the immune system turns towards the body itself causing autoimmune diseases such as Juvenile diabetes, Lupus, and rheumatoid arthritis.

During their search through thousands of compounds they found that the known cancer drug, Cisplatin, a drug containing the metal platinum, directly stripped foreign molecules from the MHC class II protein. From there, they found that platinum was just one member of a class of metals, including a special form of gold, that all render MHC class II proteins inactive.

In subsequent experiments in cell culture, gold compounds were shown to render the immune system antigen presenting cells inactive, further strengthening this connection. These findings now give researches a mechanism of gold drug action that can be tested and explored directly in diseased tissues.³⁸

Such kind of mode of action for Ayurvedic Swarna Bhasma is urgently needed for more scientifically validated therapeutic application of all these formulation containing Swarna Bhasma of Ayurveda.

Caution

Many authorities of subject are continuously indicating cautions in application of nano particles. Development of novel nano particles must be followed by the assessment of their potential risks on life and environment, and possible remedial measures.³⁹

CONCLUSION

A critical analysis of all available facts suggest very prominently that Swarna Bhasma is a wonder drug of Ayurveda which may be calibrated on parameters of contemporary science as researchers are adding new substantiated vision in case of Gold compounds all across globe in service of humanity.

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