



CODEN [USA]: IAJPBB

ISSN: 2349-7750

**INDO AMERICAN JOURNAL OF
PHARMACEUTICAL SCIENCES**Available online at: <http://www.iajps.com>

Review Article

**REVIEW ON THERAPEUTIC POTENTIAL OF AYURVEDIC
MEDICINE SWARNABHASMA (INCINERATED GOLD)**Trupti S. Patil¹ and Asmita A. Wele²

¹BAMS MD, Assistant Professor, Department of Rasashastra and Bhaishajyakalpana,
BVDU College of Ayurved, Bharati Vidyapeeth Deemed University,
Pune, 411043, India. Contact no: +91 9822316623, +9120 24373954

²BAMS, MD, Professor, Ayurveda Chair, University of Debrecen,
Debrecen, Hungary, Email ID-asmita.wele@gmail.com

Abstract:

Gold is an important medicinal ingredient known to render rejuvenation and longevity as stated by ancient Ayurvedic literature. Research based on gold bhasma has led to evidence regarding physico chemical nature of the drug, revealing nano-size and unique nature of gold particles in it. A pubmed search was performed to identify all relevant researches based on gold bhasma, and related work on gold nanoparticles. Sanskrit literature regarding Gold was referred to elaborate the drug delivery systems of gold bhasma. The explored and unexplored facts have been highlighted for further researches in this area. There is adequate safety data about cell -friendly nature of gold bhasma as evident by in-vitro experiments. Its safety is also established by toxicity study. The next areas for exploration should be bioavailability and to know the mechanism of action. This review also puts forth unique drug delivery systems of Ayurveda where the accompanying drugs play important role.

Keywords: *Ayurveda, Swarna, Traditional Indian Medicine, Bhasma, gold nanoparticles, cancer, bioavailability*

Corresponding Author:**Dr. Trupti S. Patil,**

BAMS, MD,

Assistant Professor,

Department of Rasashastra and Bhaishajyakalpana,

BVDU College of Ayurved,

Bharati Vidyapeeth Deemed University,

Pune, 411043, India

Contact no +91 9822316623, +9120 24373954

QR code



Please cite this article in press as Trupti S. Patil and Asmita A. Wele., *Review on Therapeutic Potential of Ayurvedic Medicine Swarnabhasma (Incinerated Gold)*, Indo Am. J. P. Sci, 2018; 05(01).

INTRODUCTION:

The noble metal Gold [Swarna] has been used since time immemorial for coinage, jewellery and medicinal purposes. Ayurveda, the ancient Indian medicine mentions about incredible therapeutic potential of gold. It is one of the few metals which can be used at nano scale due to its resistance to oxidation. Gold nanoparticles have therapeutic applications in cancer [1, 2, 3]. With the size of about one hundred to ten thousand times smaller than human cells, nanoparticles can offer unprecedented interactions with biomolecules both on the surface of and inside the cells, which may revolutionize cancer diagnosis and treatment [4].

It has been reported that Ayurvedic medicine 'Gold bhasma' also comprises of nanoparticles of gold metal, of around 28-60 nm [5, 6, 7, 8, 9] apart from few other elements in major or trace levels [10, 11]. The composition of gold bhasma varies, as the manufacturing process varies. It is possible to explore details about bhasma particles by sophisticated instrumental techniques like X Ray Diffraction [XRD], Atomic Absorption Spectroscopy [AAS], Transmission electron microscopy [TEM], Field emission surface electron microscopy [FESEM], Atomic force microscopy [AFM], Inductively coupled plasma mass spectroscopy [ICP MS], Inductively coupled plasma atomic emission spectroscopy [ICP AES], Nuclear magnetic resonance imaging [NMR], Fourier transform infra red [FTIR] etc. In vitro studies have aimed to assess safety of gold bhasma in human cells.

Gold has been used in various forms till date for medicinal purposes. In the decade of 1990 pharmacology of Gold compounds like Auranofin and Gold sodium theomalate was explored. Auranofin is known for its efficacy in rheumatoid arthritis [12,13], tuberculosis and as a nervine drug [14] Gold sodium theomalate has been used as a anti-rheumatic drug. However their use has been limited due to high incidence of side effects [1]. The balance between therapeutic potential and safety has been well established by Ayurveda as evident through years of clinical practice [15]. Gold bhasma is commonly used in India since ancient time [15]. This paper reviews the investigations on gold bhasma, and Ayurvedic literature to set future trend of research.

MATERIALS AND METHODOLOGY:

Literature search was conducted by screening published research papers indexed on Pubmed, and Scopus databases, using the key words *Swarna*, Gold, Bhasma, Ayurvedic gold formulations, Characterization of gold bhasma, gold nanoparticles till September 2017. The research papers on Swarna Bhasma focusing on

characterization, cellular uptake, toxicity etc have been assessed for quality and selected articles have been included in this review. Related Ayurvedic literature in Sanskrit language, and published books in Sanskrit, Hindi and Marathi were referred, and existing trends have been considered for this review to highlight unexplored areas.

Trends in Ayurveda Regarding Direct Medicinal Use of Pure Gold -

Ayurvedic physicians have been using pure gold (24 carat) directly through the following practices. Pure 24 carat gold rubbed in circular manner on a smooth stone [*Sahan*] with ghee or honey is administered orally to newborn, with documented claim to enhance baby's intellect, memory and immunity [16]. There is no standardization of this technique and unknown remains the mechanism of action. Whether the rubbed gold releases gold particles in characterizable form is a subject of investigation. Safety and efficacy of similar practice has been reported [17,18] where instead of rubbed gold, bhasma of gold had been used [19]. Rubbed gold is claimed to protect body from toxins and treat infertility in women [19].

Secondly, it is advised to pregnant ladies to drink water which has been boiled with pure gold chip; for beneficial effects on growing fetus. Such practice is also recommended in normal persons for improving overall health, strength and immunity. Whether gold ions are released into water or any change is brought about in water at subtle level after boiling with pure gold is unexplored. Size dependent translocation of gold nanoparticles from maternal blood into the fetus in pregnant rats [20] clarifies that gold nanoparticles are transferred from mother to foetus. Their action in foetus is unknown.

Gold Bhasma [Swarnabhasma / incinerated gold]

Gold bhasma is an ancient Ayurvedic incinerated formulation [19, 21, 22] in the form of light brown, pink or black colored fine powder [15]. Its particles are characterized by ability to float over water surface [*Varitaratwa*]. Gold bhasma is administered with various media like cow ghee, black pepper, honey, medicated ghee, medicated milk etc [Table 3]. About 18 different methods are reported in Ayurvedic literature for manufacturing gold bhasma [Table 1]. Since ancient time, Ayurvedic physicians have been using gold bhasma to treat asthma, wasting of muscles, mental disorders and as rejuvenator and aphrodisiac, to enhance vigour, vitality, memory, intellect, immunity, and longevity [15, 19, 20, 21, 22, 23].

Process of Conversion of Pure Gold In Gold Bhasma -

The breakdown from metal to bhasma form is done by detoxification, trituration and incineration [*Shuddhi* and *Maran* respectively]. Bhasmas in general have been reviewed to highlight the processes involved [24, 25]. For *shuddhi*, Pure Gold is pressed to make thin foil. Then it's heated on a strong flame until red hot and quenched sequentially for 7 times each in sesame oil, buttermilk, cow urine, acidic ferment of rice, also known as sour gruel (*Kanji*) and decoction of Dolichous biflorus Linn. [Leguminosae] [22]. another process involves heating of gold till it turns red and quenching thrice in decoction of Bauhinia

variegata Linn [Leguminosae]. After this step the incinerations are done in controlled environment in sealed earthen- crucibles using cowdung cakes in traditional kilns or pits, known as '*Puti*' in Sanskrit. Repeated cycles of trituration and heating, and pounding convert it into gold bhasma. The herbal drugs are used for trituration after each heating [incineration] . The process is lengthy and tedious. The natural entities viz air, water, heat, inorganic and organic compounds involved, play a role in the conversion. Variations of processing ingredients, process specifications for making of Gold bhasma are tabulated in Table 1, which is based on ancient Ayurvedic manuscripts.

Table 1: Various Ingredients Which Are Incinerated By Compounding With Gold For Making Gold Bhasma -

Gold bhasma, making process Serial no.	Ingredients which are incinerated systematically after being triturated	Reference of Ayurveda literature
1.	- Gold [<i>Shuddha</i>] -Rasasindura(Formulation of Hg and S) -Juice of Citrus medica [Rutaceae]	[22]
2.	-Gold [<i>Shuddha</i>] -Rasasindura -Cinnabar [<i>Shuddha</i>], -Juice of Citrus medica [Rutaceae]	[19, 22]
3.	-Gold [<i>Shuddha</i>] -Mercury [<i>Shuddha</i>] -Juice of Citrus medica [Rutaceae]	[22]
4.	-Gold [<i>Shuddha</i>] -Mercury [<i>Shuddha</i>] -Sulfur [<i>Shuddha</i>] -Juice of Citrus medica [Rutaceae]	[19, 26, 27]
5.	-Gold [<i>Shuddha</i>] -Copper pyrite[<i>Shuddha</i>] -Lead[<i>Shuddha</i>] -Juice of Calotropis procera Ait. [Asclepiadaceae]	[26]
6.	-Gold [<i>Shuddha</i>] -Mercury [<i>Shuddha</i>] -Copper pyrite [Shuddha]	[26]
7.	-Gold [<i>Shuddha</i>] -Mercury [<i>Shuddha</i>] -Lead [Shuddha]	[26]
8.	-Gold [<i>Shuddha</i>] -Asafoetida -Cinnabar -Latex of Euphorbia nerifolia Linn. [Euphorbiaceae]	[26, 27]
9.	-Gold [<i>Shuddha</i>] -Mercury [<i>Shuddha</i>] -Cinnabar [<i>Shuddha</i>] -Juice of Citrus medica [Rutaceae]	[19]
10.	-Gold [<i>Shuddha</i>] -Mercury [<i>Shuddha</i>]-Cinnabar [<i>Shuddha</i>] -Sulfur [<i>Shuddha</i>] -Realgar [Shuddha]	[19]

	-Ammonium chloride -Juice of Citrus medica [Rutaceae]	
11.	-Gold [<i>Shuddha</i>] -Mercury [<i>Shuddha</i>] -Realgar [<i>Shuddha</i>] -Rasasindura -Swarnamakshik bhasma -Juice of Citrus medica [Rutaceae]	[19]
12.	-Gold [<i>Shuddha</i>] -Mercury [<i>Shuddha</i>] -Realgar [<i>Shuddha</i>] -Rasasindura - -Juice of Citrus medica [Rutaceae] -Latex of Calotropis procera Ait [Asclepiadaceae]	[19]
13.	-Gold [<i>Shuddha</i>] -Mercury [<i>Shuddha</i>] -Magnesium Silicate -Sulfur, [<i>Shuddha</i>] -Juice of Citrus medica [Rutaceae] -Decoction of Bauhinia variegata Linn. [Leguminosae]	[19]
14.	-Gold [<i>Shuddha</i>] -Lead [<i>Shuddha</i>] -Juice of Citrus medica [Rutaceae]	[27]
15.	-Gold [<i>Shuddha</i>] -Asafoetida -Cinnabar [<i>Shuddha</i>] -Sindura [<i>Shuddha</i>] -Realgar [<i>Shuddha</i>] -Decoction of Bauhinia variegata Linn. [Leguminosae][Sanskrit name: <i>Kanchanar</i>]	[27]
16.	-Gold [<i>Shuddha</i>] -Mercury [<i>Shuddha</i>] -Sulfur [<i>Shuddha</i>]-Bauhinia variegata bark-Seal in crucible prepared using paste of Bauhinia variegata Linn. [Leguminosae]	[27]
17.	-Gold [<i>Shuddha</i>] -Heated and quenched in juice of herb ' <i>Jwalamukhi</i> ', and triturated with juice of same herb.	[28]
18.	-Gold [<i>Shuddha</i>] -Rasaparni - Hingul [<i>Shuddha</i>] -Lemon juice	[28]

The chemical composition, color, particle size of final product is expected to vary according to variation in process. The role of key ingredients in the above mentioned processes needs exploration. Mercury, Cinnabar, Lead oxide etc have been used along with gold, and herbal drugs like lemon, asaphoetida. There are few gaps regarding number of incinerations, quantity of fuel, and quantity of ingredients; and hence process **standardization** is needed, so that the final product is of desired quality. Selection of raw drugs is important too

considering the minerals involved which do have geological variations.

Over the last decade, research has led to certain conclusions regarding the physicochemical nature of gold bhasma, which are presented in table 2. [5, 6, 7, 8, 9, 10, 11].

Table 2: Known facts regarding Characterization of Gold Bhasma

S.N.	Major findings regarding characterization of finished product Gold Bhasma	Process of detoxification [<i>Shodhan/ Shuddhi</i>] of gold	Process of incineration [making process of Gold Bhasma]	Reference
1.	-Analysis of gold bhasma by AAS- 92% gold -Mercury absent, no traces -TEM :57nm particle size -AFM :56 nm particles size -Globular morphology FTIR - no organic compounds XRD - identical to pure gold	Heating gold foil red hot and dipping in liquids viz sesame oil, buttermilk, cow urine, sour gruel and decoction of Dolichos biflorus Linn, 7 times in each of the liquid .Next process was application of paste of hematite and rock salt on gold foil, and it was incinerated in earthen crucible case for 1.30 hr over strong heat [~1000 C]	Gold + Mercury + Sulfur-amalgamation - heating in a closed crucible using 30 cowdungs [42 times] Temperature - 900 ⁰ C each time	[6]
2.	-Analysis of gold bhasma by AAS Gold 20.34% Iron 39.09 % Arsenic 0.17 % Barium 0.33 % Calcium 1.96 % Magnesium 2.08 % Lead .03 % Zink 74 ppm Nickel 75 ppm -IR spectra rules out presence of organic compound in bhasma -Particle size - not reported	Heating gold red hot and dipping in liquids viz sesame oil, buttermilk, cow urine, kanji and decoction of Dolichos biflorus Linn, 7 times in each of the liquid .	Gold+ red lead [Pb3O4] + realgar [As2S2] - pounded with latex of Calotropis gigantea- heating by cowdung cakes, repeated till fine powder floats on water Temperature - 1000 degree C each cycle	[7]
3.	Particle size calculated by Scherrer formula from XRD pattern -28-35 nm. Total gold percentage not reported No investigation using TEM	Market sample. Process of making is not mentioned.	Not reported	[8]
4.	Particle size 1-10 Micrometer , Percentage of Gold - 52.33% Arsenic -0.3 % Mercury- 0.05 % [ICP OES]	Not mentioned	Process is not mentioned	[11]
5.	Particle size of gold bhasma - 7.55 to 9.97 microns , by Particle size determination [Malveran] . XRD , FTIR prove that gold bhasma is mainly pure gold.	Not mentioned	Gold+ mercury - amalgamation, and incineration with leaf of Ricinus communis and sulfur using 30 cow dung cakes. Total 14 incinerations at 800 °C , addition of sulfur was done each time. Final product was triturated with juice of Aloe vera and heated at 70 degree C	[10]
6.	ICP MS [presence of Mg, Ca, Fe, Si, Mn, Ni, As] SEM EDS DLS XRD [Particle size 60 nm]	Not mentioned	Not mentioned	[5]

Table 2- Primary data on researches on bhasma of gold

Brown et al., 2007 [6], studied physicochemical nature of Swarna bhasma, manufactured by a method involving amalgamation of gold with mercury. AAS confirmed the absence of Hg in the final sample of gold bhasma. In this study presence of nanoparticles of gold was clearly reported, which is evident by transmission electron microscopy and atomic force microscopy. Spherical nature of bhasma particles is also evident. At about 900 Degree Celsius temperature mercury may get evaporated, leaving no traces in gold bhasma. AAS confirmed presence of 92 % elemental gold. As a next step for exploration, in process testing during and after each cycle of incineration can help us understand the exact role of mercury in process of conversion of Au into AuNP, of 57 nm as confirmed by TEM and reconfirmed by AFM. Further research using Thermogravimetric tests, AAS, ICP MS, differential thermal analysis during process can lead to exact understanding of process. Analysis of earthen vessels can elaborate on any absorbed elements in its fine pores.

Thakur et al [10] studied gold bhasma made using Hg, Au and S, by few of the characterization techniques to highlight spherical and irregular particles of gold. The study reports 98% Gold in gold bhasma by elemental assay, along with presence of traces of Ag, Fe, Cu, Zn as evident by AAS. AAS has not been used for determination of Au percentage in this study. The particle size has been determined by Malvern Mastersizer, reported to be 7.55- 9.97 microns, and this study has concluded presence of few nano particles in agglomerated form. There is no detailed exploration of said nanoparticles in present study, by TEM or AFM.

X ray diffraction study of gold bhasma [6, 10] confirmed that this type of bhasma prepared using mercury is pure gold, and not oxide or sulphide of gold unlike few other metallic bhasmas. As gold is a noble metal, known to be resistant to oxidation and corrosion, its nano form is unique. Interestingly during bhasma formation process the gold is converted to small particles which are of pure gold, but have brownish color. Other properties of these particles, like surface charge, magnetism [if any], agglomeration tendency, and melting point [if it were reduced than bulk gold] need exploration. At the same time, gold bhasma prepared from cinnabar and other methods needs to be compared with that formed by Au-Hg amalgamation method. It is known that properties of matter change at nano scale in a weird way, which makes the nanoparticles in bhasma form safe for medicinal use.

Lead oxide has been used as one of the ingredients to make gold bhasma [22]. Primary data about this particular method shows, when lead oxide and realgar were used to manufacture gold bhasma, it consisted of 20 % elemental gold [7], which is very less as compared to methods involving mercury. The other elements in this type of bhasma are iron [39.09%], arsenic [0.17 %], barium [0.33 %], calcium [1.96 %], magnesium [2.08 %], lead [0.03 %], zinc [74 %], nickel [75 ppm]. It is clear that each type of gold bhasma is different, and pharmaceutical standardisation is necessary for all reported processes. 39% iron comprises of the maximum part of this type of gold bhasma. The source of this high amount of iron in gold bhasma is not traceable in the raw drugs used, i.e. red lead [compound of lead and oxygen], realgar [compound of arsenic and sulfur], gold, and *Calotropis gigantea*. This calls for a need of raw mineral standardisation as well, as there is great diversity in various market samples of minerals like realgar, mica etc. In this case, a process standardisation and in process analytical testing can lead to exact understanding of process. The traces of arsenic [0.17 %] have been reported, and further one or two cycles of incinerations may lead to removal of these levels by volatilising from gold bhasma. Unless the final composition is known, exact pharmacology of such multi-element drugs would be unknown and unimaginable. The mortar and pestle used may get eroded during trituration and some elements from it can get added in final product. It is highly recommended to use instruments made up of good quality iron.

Khedekar et al. [11] have also documented findings about gold bhasma, but the exact making process is not mentioned clearly. This study reported the size of Gold Bhasma to be 1-10 micrometer by SEM, and 52.33 % elemental gold in the drug. Ingredients and Manufacturing process have not been mentioned. The drug has been prepared by one of the formulae for preparation of gold bhasma from text *Rasatarangini*. Other important characterization techniques like XRD, TEM have not been used leaving behind many unknown questions. Apart from Gold 52.33%, Arsenic -0.3 %, Mercury- 0.05 %, the rest of composition of the drug can not be understood from the data. A technique like ICP MS and EDXRF, FTIR can give more insights into knowing the details.

Compound Formulations of Gold - [Herbominerals]

Gold in the form of gold bhasma or foil is an ingredient [29] of many formulations like *Brahmi Vati* and *Saraswatarishta* which are used to combat brain ageing [30], decline in cognitive function, anxiety and insomnia due to depression. There is primary evidence for anti-anxiety and anti-

depressant action of gold formulations [31]. The drug-organ affinity concept is well accepted in modern pharmacology. Gold is said to have affinity towards heart, brain, sperms, and overall vitality due to nourishment to *Shukradhatu* [15, 22]. Gold has been detected in human sperms, showing the affinity to sperms [32,33]. Ayurveda regards it as a *Shukra vardhak* drug, improving the quality and quantity of *Shukradhatu*, comparable to semen [15, 26].

Gold is one of the ingredients in formulations like *Makardhwaj*, *Sutashekhar*. The drug *Sutashekhar*, which contains gold, has been well known in India for treating hyperacidity and gastric pain [15, 34] before the era of new age hyperacidity medicaments. *Makardhwaj* is a formulation which is used as aphrodisiac and rejuvenating action [15]. There are numerous other formulations of gold, which need exploration.

Modern Day Gold Nanoparticles [Au NPs]-

Nanomaterials [1-100 nm] have similar size as that of basic biological unit DNA, making them highly applicable in biological field [35]. Preclinical and clinical studies of gold nanoparticles for cancer treatment [2; 3] are evident. Application of AuNP for detection of cancer [2] is done.

Scientists today are engaged in various studies on gold nanoparticles prepared by chemical reduction, where main challenge is of toxicity of the nanoparticles [1, 36, 37]. Scientists are in search for novel greener methods for synthesis of AuNPs. [1, 38, 39, 40, 41]. There is a sizeable data showing the antibacterial activity of silver and gold nanoparticles prepared using plants like *Mentha piperita* [Lamiaceae], *Tribulus terrestris* [Zygophyllaceae] and *Sesbania grandiflora* [Fabaceae] [42]. Ayurveda already mentions 18 different methods of making gold bhasma, [Table 1] which need systematic exploration. The ingredients do or do not express themselves in final

product, some of elements escape in gaseous elemental or compound form.

Toxicity studies –

Mitra et al., 2002 [7], apart from characterization of gold bhasma prepared using lead metal; also studied its acute, sub-acute and chronic toxicity in albino mice. It shows no evidence of toxicity in mice, at a human dose of 30 mg which was extrapolated for mice.

Administration of Gold Bhasma -

Bhasma is mixed with certain media just before consumption by patient. There are 61 different combinations of gold bhasma in literature of Ayurveda. This includes medicated ghee processed with *Acorus calamus* [Acoraceae], *Aegle marmelos* [Rutaceae], medicated milk processed with blue lotus, milk, powder of *Embllica officinalis* [Phyllanthaceae], medicated ghee with *Asparagus racemosus* [Asparagaceae], juice of *Bacopa monniera* [Scrophulariaceae], honey etc [19, 21].

Depending on specific target action expected, Ayurvedic physicians use specific medium. The dispersion in ghee or honey may be useful to release the agglomeration of gold particles and to help in better absorption. It is documented in *Rasayogasagar* [21] that gold bhasma when administered with *Saussurea lappa* [Asteraceae], *Acorus calamus* [Acoraceae], honey and ghee enhances intellect, strength and decision making skill of children and adolescents. Gold nanoparticles are reported to act like drug carriers, and this idea has been extensively practiced in Ayurved since ancient time. Table 3 mentions the data from Ayurvedic literature, which is based on Ayurvedic pharmacology, where accompanying drugs are considered to be most important in target action as well as synergistic action. For instance, different Medicated ghee have been used for activity on CNS where crossing of blood brain barrier is necessary.

Table 3: Accompanying Medicaments and the Ethnopharmacology of Gold Bhasma , and Rubbed Gold

Serial no.	Form of Swarna [Gold]	Accompanying drug or medium	Indication as per literature of Ayurveda	Reference
1.	Swarna Bhasma	<i>Black pepper and ghee [Marich and Ghruta]</i>	Longevity [Ayuwardhak], rejuvenator [Rasayan], aphrodisiac [Vrishya], enhances intellect [Buddhivardhak], enhances memory [Smrutivardhak], improves <i>Shukradhatu</i> [Viryavardhak], strengthening [Kshinanam Pushtikari], etc	[22]
2.	'Suvarna'	<i>Acorus calamus [Vacha]</i>	Improvement of intellect [Medha vardhak]	[27]
3.	'Suvarna',	<i>Nelumbo nucifer [Padmakesar]</i>	Enhancer of skin beauty [Kanti vardhak]	[27]

4.	'Suvarna',	<i>Convolvulus pluricaulis</i> [Shankhapushpi]	Longevity [Ayuwardhak]	[27]
5.	'Suvarna',	<i>Pueraria tuberosa</i> [Vidari]	Praja janana [helps reproductive function]	[27]
6.	Varkha	Butter, sugar, honey	Useful to treat wasting of body [Kshaya]	[27]
7.	'Suvarna',	Honey and <i>Emblica officinalis</i> [Amalaki]	Useful for vitalizing critical patient [life saver]	[27] [43]
8.	Pure gold ie Apakwa Swarna [24 carat gold] in rubbed form	Honey and water	Toxicity [Visha]	[27]
9.	Suvarna churna	<i>Bacopa monnieri</i> , <i>Acorus calamus</i> , <i>Saussuria lappa</i> , <i>Convolvulus pluricaulis</i> respectively [Brahmi swaras, Vacha, Kushtha, Shankhapushpi in form of nasya/ anjan/ pana]	Mental disorders, epilepsy [Unmad, Chittabhrama, Apasmar, Bhutabadha]	[27]
10.	'Suvarna',	<i>Nelumbo nucifer</i> [Padmabija], Honey [Madhu], Laja, <i>Callicarpa macrophylla</i> [Priyangu], Cow milk	Longevity [Alakshminashak]	[27] [43]
11.	'Suvarna'	Ghee processed with <i>Asparagus racemosus</i> [Shatawari Ghruta]	Rejuvenator and aphrodisiac [Rasayan Vajikaran]	[27] [43]
12.	'Suvarna'	<i>Nelumbo nucifera</i> [Padma], <i>Nymphaea cyanea</i> [Nilotpala] Kwath, <i>Glycerrhiza glabra</i> [Yashti], Siddha Ghee, and milk	Rejuvenation, longevity [Rasayan, Vayashthapak]	[27] [43]
13.	Gold bhasma	Bark of <i>Aegle marmelos</i> [Bilwa twak], Rasasindur [Formulation of mercury and sulfur]	Vataj Jwar	[19]
14.	Gold bhasma	<i>Rungia parviflora</i> [Parpat], Rasasindura	Pittaj Jwara	[19]
15.	Gold bhasma	<i>Ocimum sanctum</i> [Tulasi], Rasasindura	Kaphaj Jwara	[19]
16.	Gold bhasma	Abhrak bhasma, honey [madhu]	Jirnajwara	[19]
17.	Gold bhasma	<i>Aegle marmelos</i> [Bilwa], <i>Cuminum cyminum</i> [Jirak]	Diarrhea [Atisar]	[19]
18.	Gold bhasma	Rasaparpati [formulation of mercury and sulfur]	IBS or colitis [Grahani]	[19]
19.	Gold bhasma	<i>Tinospora cordifolia</i> [Guduchi sattwa], loha bhasma	Pandu	[19]
20.	Gold bhasma	Bhasma of mica [Abhrak bhasma] / rasasindura / [Bhasma of pearls] Mouktika bhasma	Rajayakshma	[19]
21.	Gold bhasma	<i>Lilium polyphyllum</i> [Kshirakakoli], <i>Smilax glabra</i> [Chopachini]	Shuddhi of Uterus [Garbhashay shodhan]	[19]
22.	Gold bhasma	Guduchi, <i>Crocus sativus</i> [kesar], <i>Hemidesmus indicus</i> [Sariva]	Purifies blood [Raktashodhan]	[19]
23.	Gold bhasma	Rasapushpa [a mercurial formulation]	Syphilis [Firanga]	[19]
24.	Gold bhasma	<i>Hedychium spicatum</i> [Shathi]	Asthma [Shwasa]	[19]
25.	Gold	<i>Emblica officinalis</i> [Amalaki]	Hyperacidity [Amlapitta]	[19]

	bhasma			
26.	Gold bhasma	<i>Rasasindura, Euphorbia dracunculoids [Shankhini]</i>	Epilepsy [Apasmar]	[19]
27.	Gold bhasma	<i>Rasasindur, Sida cordifolia [Bala]</i>	[Shirsha vepathu] Parkinson like signs	[19]
28.	Gold bhasma	<i>Boerhavia diffusa [Punarnava], Kajjali [formulation of mercury and sulfur], Cows urine [Gomutra]</i>	<i>Mushkashotha [Hydrocele like condition]</i>	[19]
29.	Gold bhasma	<i>Vitis vinifera [Draksha], Piper longum [Pippal]i, Myrica nagi [Katphal], Glycerrhiza glabra [Yashti], Madhu [Honey]</i>	Improves the quality of voice [Swarya]	[19]
30.	Gold bhasma	<i>Pterocarpus santalinus [Raktachandan], Nagkeshar/ Kamal Kesar, Nelumbo nucifera [Utpal], Yashti, Sugar [Sita], Rubia cordifolia [Manjishtha], Crocus sativus [Kesar]</i>	<i>Lavanyavridddhi [beauty enhancer]</i>	[19]
31.	Gold bhasma	<i>Zingiber officinalis [Shunthi], Syzygium aromaticum [Lavang], Piper nigrum [Marich], Madhu [honey]</i>	Schizophrenia [Unmad]	[19]
32.	Gold bhasma	<i>Embllica officinalis [Amalaki] churna, Bhavana of Gayatri Swaras</i>	<i>Arishta lakshan</i>	[19]
33.	Gold bhasma	<i>Acorus calamus [Vacha], Tinospora cordifolia [Guduchi], Zingiber officinalis [Shunthi], Asparagus racemosus [Shatawari], for 6 months duration</i>	Improves intellect [Medha vridddhi]	[19]
34.	Gold bhasma	<i>Shaliparni, Vidari, Ashwagandha, Kapikacchu for 3 months duration</i>	<i>Improves muscles [Mansajanan, Deha Pushtikara], Prajajanana</i>	[19]
35.	Gold bhasma	<i>Embllica officinalis [Amalaki], Desmodium gangeticum [Shaliparni], Zingiber officinalis [Shunthi], Boerhavia diffusa [Punarnava]</i>	<i>Rejuvenator [Rasayan], strengthening [Balya], anti aging</i>	[19]
36.	Gold bhasma	<i>Jivaniya gana ie 10 drugs viz. Microstylis wallichi [Jivaka], Microstylis muscifera [Risabhaka], Polygonatum verticillatum [Meda], Polygonatum verticillatum [Mahameda], Roscoea procera [Kakoli], Roscoea procera [Ksirakakoli], Phaseolus trilobus [Mudgaparni], Teramnus labialis [Masaparni], Leptadenia reticulate [Jivanti], Glycyrrhiza glabra Linn / Liquorice [Yashtimadhu]</i>	<i>anti aging [Jivaniya]</i>	[19]
37.	Gold bhasma	<i>Mesua ferrea [Nagkesar] [to be consumed at period of ovulation ie Rutukala]</i>	<i>Garbhadharana [helps in conceiving baby]</i>	[19]
38.	Gold bhasma	<i>Kakolyadi gana - Roscoea procera [Kakoli], Roscoea procera [Ksirakakoli], Microstylis wallichi [Jivaka], Microstylis muscifera [Risabhaka], Polygonatum verticillatum [Meda], Polygonatum verticillatum [Mahameda], Tinospora cordifolia</i>	<i>improves lactation in lactating mothers [Stanyavridddhi]</i>	[19]

		<i>[Chhinna-ruha], Pistacia integerrima [Karkata-Shringi], Bambusa arundinaceae [Tugakshiri], Nelumbo nucifera [Padmaka], Habernaria intermedia [Riddhi], Vriddhi, Raisins [Mridvika], Leptadenia reticulata [Jivanti] and Glycerrhiza glabra [Madhuka]</i>		
39.	Gold bhasma	<i>Suvarnamakshik bhasma [bhasma of copper pyrite] and sugar</i>	<i>toxins [Vishabadha]</i>	[19]
40.	Gold bhasma	<i>Suvarnamakshikbhasma [bhasma of copper pyrite] and Delphinium nudatum [Nirvishi]</i>	<i>toxins [Vishabadha]</i>	[19]
41.	Gold bhasma	<i>Stereospermum suaveolens [Patala], Madhu [honey]</i>	<i>hiccups [Hikka]</i>	[19]
42.	Gold bhasma	<i>Sitopala [Sugar]</i>	<i>Rickets, Asthishodha, Asthigata kshata, Asthivakrata in babies</i>	[19]
43.	Gold bhasma	<i>Acorus calamus or Nordostachys jatamansi [Jatila]</i>	<i>Vitiation of Vata in head , resulting in headache [Shirsha vata]</i>	[19]
44.	Gold bhasma	<i>Loha bhasma and Abhrak [mica] bhasma , decoction of Crataeva nurvala [Varun]</i>	<i>Renal inflammation [Vrukka roga, Vrukka daha shotha]</i>	[19]
45.	Gold bhasma	<i>Black bitumen [Shilajatu], Rajat [silver] bhasma</i>	<i>Placental abnormalities [Jarayu Shwayathu]</i>	[19]
46.	Gold bhasma	<i>Abhrak bhasma and Loha bhasma [bhasma of mica and bhasma of iron]</i>	<i>Jatharastha Mala , vata shamak</i>	[19]
47.	Gold bhasma	<i>Curcuma longa [Haridra], Boerhavia diffusa [Punarnava] , Zingiber officinalis [Juice of fresh ginger]</i>	<i>Mushkashotha [Vrushan shotha] [inflammation of testis]</i>	[19]
48.	Suvarna [its form unspecified]	<i>Aegle marmelos [Bilva], ghee, honey [for one year duration]</i>	<i>Rejuvenator [Alakshmi nashan , rasayan]</i>	[21, 43]
49.	Suvarna	<i>Kamalbija, madhu, laja, Priyangu, Godugdha</i>	<i>Rejuvenator [Alakshmi hara, Rasayan]</i>	[21, 43]
50.	Suvarna	<i>Nymphaea cyanea [Nilotpaladala], and sesame kshirapaka [Cows milk medicated with the said drugs]</i>	<i>Rejuvenator [Alakshmi nashak, Rasayan]</i>	[21, 43]
51.	Suvarna	<i>Honey, Emblica officinalis [Amalaki powder]</i>	<i>Pranasanshayat [in critically ill patient]</i>	[21, 43]
52.	Suvarna	<i>Ghee medicated with Asparagus racemosus [Shatawari Ghruta] , honey</i>	<i>Rejuvenator [Rasayan]</i>	[21, 43]
53.	Suvarna	<i>Callycarpa macrophylla [Gochandan], Mohanika [Controversial] , Glycerrhiza glabra [Madhuka], Honey</i>	<i>Rejuvenator [Rasayan]</i>	[21, 43]
54.	Suvarna	<i>Decoction of Nymphaea cyanea [Nilotpala kwatha] , Glycerrhiza glabra [Yashti], Ghee, Cow milk</i>	<i>For longevity, rejuvenator [Rasayan, Ayushyavardhak]</i>	[21, 43]
55.	Suvarna	<i>Emblica officinalis fruit powder</i>	<i>Life saver, useful in critically ill patient [Arishtanashak]</i>	[21, 43]
56.	Kanaka Raja [gold bhasma]	<i>Sugar ,Acorus calamus [Vacha], Emblica officinalis [Amalaki], Combination of Emblica officinalis, Terminalis chebula and Terminalia belerica fruits [Triphala], Ghee.</i>	<i>Rejuvenator [Rasayan]</i>	[21, 43]

57.	Suvarna Churna [gold bhasma]	<i>Bacopa monnieri [Brahmi]</i> , <i>Acorus calamus [Vacha]</i> , <i>Saussuria lappa [Kushtha]</i> , <i>Convolvulus pluricaulis [shankhapushpi]</i>	<i>Mental disorders, epilepsy [Unmad, Apasmara, Bhutabadha, other manasvyadhi]</i>	[21, 43]
58.	Suvarna Churna [Swarna bhasma]	<i>Saussuria lappa [Kushtha]</i> , <i>Honey</i> , <i>Ghee</i> , <i>Acorus calamus [Vacha]</i>	<i>Physical strength, intellect and Memory enhancer in children and adolescents [Vapu, Medha, Bala, Bala, Buddhi vardhak in children]</i>	[21]
59.	Suvarna Churna [Swarna bhasma]	<i>Alternanthera sessilis [Matsyaksha]</i> , <i>Convolvulus pluricaulis [Shankhapushpi]</i> , <i>Honey and Ghee</i>	<i>Vapu, Medha, Bala, Bala, Buddhi vardhak [Physical strength, intellect and Memory enhancer in children and adolescents]</i>	[21]
60.	Kanak Churna [Swarna bhasma]	<i>Holostemma creeper [Arkapushpi]</i> , <i>Acorus calamus [Vacha]</i> , <i>Honey</i> , <i>Ghee</i>	<i>Vapu, Medha, Bala, Bala, Buddhi vardhak [Physical strength, intellect and Memory enhancer in children and adolescents]</i>	[21]
61.	Suvarna Churna [Swarna bhasma]	<i>Myrica nagi [Kaitarya]</i> , <i>Cynodon dactylon [Shwetadurva]</i> , <i>Ghee</i> , <i>Honey</i>	<i>Vapu, Medha, Improves strength and intellect [Bala, Buddhi vardhak] [Physical strength, Intellect and Memory enhancer in children and adolescents]</i>	[21]

As elaborated in the table 3, many rejuvenating herbs, honey, ghee, medicated milk and ghee etc have been used as accompanying medicaments over the years in Ayurveda, with gold bhasma. Administration of gold bhasma for as long as 20 years is recommended in Rasaprakashsudhakar, to render longevity.

The effects of long term treatment using gold bhasma and its mechanism of action on various tissues and organs needs to be explored. The preventive potential of this drug, for ailments like cancer and dementia needs to be explored.

Bioavailability of gold bhasma

There is no reported study on bioavailability of gold bhasma. Tracer technique like ICP MS can be used to study absorbed gold in systemic circulation after gold bhasma therapy. It has been hypothesized that Gold nanoparticles may reach the affected site on oral administration via intestinal absorption and possibly can release Au ions in a sustained manner for therapeutic action [8]. It is documented that nano particles can also be absorbed through sublingual route directly into the blood stream. Paul et al., 2011 [8], have presumed that some Swarna bhasma particles may get absorbed through the sublingual route directly into the blood stream. Study of pharmacokinetics of Gold Bhasma will answer many questions. The accompanying media like Piper nigrum Linn [Piperaceae] [22], a bioavailability enhancer [44] may facilitate gastrointestinal absorption. The target action and cellular take up of gold may vary as the accompanying drugs vary depending on therapeutic action desired.

At present, most active area is developing gold based medicines as anti-tumour agents. [6]. Gold

nanoparticles are promising agents for cancer therapy and are being investigated as drug carriers, photo thermal agents, contrast agents and radiosensitisers [1]. Several of the currently used methods to manufacture gold nanoparticles use of toxic chemicals either in the form of reducing agents to reduce the metal salt to corresponding nanoparticles or as stabilizing agents to prevent nanoparticles from agglomeration. It is evident that synthetically or chemically prepared gold nanoparticles show hazardous effects [37]. Considering this, it is need of time to explore fully the potential of Ayurvedic gold bhasma in terms of mechanism of action and clinical applications as a rejuvenator and therapeutic drug.

Clinical Study on Gold Bhasma -

A clinical study on gold bhasma in cancer has been reported [45], however there is little reliability regarding this study as the study design is mentioned to be 'Observational'. Patients on palliative care were selected, with no mention of stage of cancer. The dose of Swarna bhasma used was 50 mg /Kg/day, which is very high dose, many fold than the recommended dose in literature and practice. This study concluded that Gold bhasma can be a potential drug for cancer treatment.

In Vitro Studies of Gold Bhasma -

Three studies have been reported of in vitro experiments using gold bhasma. Gold bhasma was

proven to be non toxic, cell friendly, compatible in the cells in which tested.

Swarna bhasma was tested in human embryonic stem cells as an in-vitro model to understand if gold could enhance self-renewal and pluripotency [46]. Swarna-bhasma having particle size of 41.1 nm reduced spontaneous-differentiation, enhanced self-renewal, pluripotency and proliferation of human embryonic stem cells [46].

Cellular entry of gold bhasma particles was tested in HeLa (human cells derived from cervical cancer) and HFF-1 (human foreskin fibroblast cells) in comparison to synthesized citrate-capped gold nanoparticles (AuNPs) [5]. Gold bhasma particles were in form of crystallites are around 60 nm in size, in form of large aggregates with a mean diameter of 4711.7 nm and some of which could enter cells. Transmission electron microscopy revealed gold bhasma particles were in vesicles, cytosol, or in the nucleus of cell. This study concluded that larger IAuPs [Bhasma of gold] entered cells via macropinocytosis, while smaller particles entered via clathrin-dependent receptor-mediated endocytosis, and the gold bhasma was safe and non toxic to cells [5].

In another study *In vitro* cytotoxicity of gold bhasma was investigated [8]. Red blood cell hemolysis, aggregation studies with blood cells, protein adsorption, complement C3 adsorption, platelet activation and tight junction permeability in Caco-2 cell line were investigated. The *Swarna bhasma* did not induce any blood cell aggregation or protein adsorption. Gold bhasma particles were also non-cytotoxic. *Swarna bhasma* particles opened the tight junctions in Caco-2 cell experiments.

The in vitro cell based studies [5, 8, 46] and animal experimentation [7] highlight the safety of gold bhasma which is also evident by thousands of years clinical practice [15].

CONCLUSIONS:

Gold is a noble metal characterised by non reactivity. Interestingly, Ayurveda reports around eighteen processes of making of gold bhasma ie Ayurvedic Nano Gold. Process dependent difference in physicochemical nature of gold bhasma has been observed. Minute processing details do affect the nature and colour of bhasma. Nano materials, due to their small size, can work at DNA levels and bring about desired changes, yet their toxicity is also reported. Ayurvedic *bhasma* manufacturing method yields nanoparticles which may be safer and tissue friendly. It may offer wide therapeutic index and applications. The debate whether nano-metals are carrier molecules or active

drugs or both is also worth exploration. The efficacy of pure Gold in rubbed particles form and gold bhasma indicates that the metal is an active molecule. When it is accompanied by herbal mixtures, decoctions, milk etc; it also acts as a carrier. There is enough scope to hypothesise that gold bhasma is an active molecule and a carrier. The ethno pharmacological literature and practical use of gold formulation in India, as well as primary evidences about nanoparticles of gold give us many leads for future exploration. The efficacy in psychosomatics disorders, cancer, arthritis, loss of vigour and vitality, infertility and prevention from toxins should be assessed.

Gold Bhasma and Gold formulations like *Brahmi Vati*, *Swamala*, and *Saraswatarishta* have a good trade in India. For wider use of gold formulations and global acceptance, systematic research based on hypotheses built upon Ayurvedic references is needed. The sublingual administration of gold bhasma and use of pure gold in rubbed form for newborn babies requires further exploration in terms of safety and efficacy profile. The preventive, promotive and curative roles of Ayurvedic forms of gold need to be explored further.

Conflicts of interest - None

ACKNOWLEDGEMENTS:

The authors are thankful to Bharati Vidyapeeth Deemed University Pune, India

REFERENCES:

- 1.Hornos C.M.F., Barbosa F Jr., 2016, Gold nanoparticles: A critical review of therapeutic applications and toxicological aspects., *J Toxicol Environ Health B Crit Rev.* 2016;19(3-4):129-48., doi:10.1080/10937404.2016.1168762.
- 2.Jain S, Hirst DG, O'Sullivan JM., 2012, Gold nanoparticles as novel agents for cancer therapy., *Br J Radiol.* 2012 Feb;85(1010):101-13. Doi: 10.1259/bjr/59448833. Epub 2011 Oct 18.
- 3.<https://www.gold.org/news-and-events/press-releases/gold-nanomedicine-clinical-trial-delivers-promising-results>].
- 4.Weibo Cai Ting Gao, Hao Hong, and Jiangtao Sun, *Nanotechnol Sci Appl.* 2008; 1: 17–32., Applications of gold nanoparticles in cancer nanotechnology,
- 5.Daniel Beaudet, Simona Badilescu, Kiran Kuruvinashetti, Ahmad Sohrabi Kashani, Dilan Jaunky, Sylvie Ouellette, Alisa Piekny & Muthukumaran Packirisamy, Comparative study on cellular entry of incinerated ancient gold particles (Swarna Bhasma) and chemically synthesized gold particles, *Scientific Reports* 7,

Article number: 10678 (2017) doi:10.1038/s41598-017-10872-3

6. Brown, C. L., Bushell, G. R., Michael W. Whitehouse, M. W., Agrawal D. S., Paknikar K. M., Tiekink, E., 2007, Nano gold-pharmaceutics: (i) The use of colloidal gold to treat experimentally-induced arthritis in rat models; (ii) Characterization of the gold in Swarna bhasma, a microparticulate used in traditional Indian medicine, *Gold bulletin* 40(3):245

7. Mitra A, Chakraborty S, Auddy B, Tripathi P, Sen S, Saha AV, Mukherjee B., 2002, Evaluation of chemical constituents and free-radical scavenging activity of Swarnabhasma (gold ash), an Ayurvedic drug., *J. Ethnopharmacol.* 2002 May;80(2-3):147-53.

8. Paul W, Sharma CP., 2011, Blood compatibility studies of Swarna bhasma (gold bhasma), an Ayurvedic drug., *Int J Ayurveda Res.* 2011 Jan;2(1):14-22. doi: 10.4103/0974-7788.83183.

9. Adhikari R., Ayurvedic Bhasmas: overview on nanomaterialistic aspects, applications, and perspectives., *Adv Exp Med Biol.* 2014;807:23-32. doi: 10.1007/978-81-322-1777-0_3.

10. Thakur Kapil, Gudi Ramacharya, Vahalia Mahesh, Shitit Shekhar, and Nadkarni Shailesh, , 2017, Preparation and Characterization of Suvarna Bhasma Parada Marit, *Journal of Pharmacopuncture*, 2017 Mar; 20(1): 36–44. doi: 10.3831/KPI.2017.20.007

11. Khedekar, S., Anupriya, Galib R, Patgiri B, Prajapati PK., 2015, Chemical characterization of incinerated gold [Swarna Bhasma] , *Advances in Applied Science Research*, 2015; 6(12):89-95

12. Paul D, 1988, Gold Therapy in the Treatment of Rheumatoid Arthritis, *Can Fam Physician.* 1988 Feb; 34: 445, 447, 449, 451-[452].

13. Roder, C., Thomson, M.J., Auranofin: repurposing an old drug for a golden new age. *Drugs R D.* 2015 Mar;15(1):13-20. doi: 10.1007/s40268-015-0083-y.

14. Richards, D.G., McMillin, D.L., Mein, E.A., Nelson, C.D., Gold and its relationship to neurological/glandular conditions., *Int J Neurosci.* 2002 Jan;112(1):31-53.

15. Gune G., Ayurvediya Aushadhigunadharmashastra-Siddhaudhadhi, Part , 3rd edition, 1933, Vaidyak Grantha Bhandar, Shaniwar Peth, Pune, India. pp 141-150

16. Sharma Hemraj, Kashyapsamhita, Sutrasthana, Lehadhyay, Kashi Sanskrit Granthamala, 4th edition 1998, Varanasi, India, PP 4,5

17. Sharma, V., Hiremath, R.R., Patil, P.A., Prasad, B.S., Safety assessment on chronic administration of Swarna Bindu Prashan— a popular Ayurvedic preparation of incinerated gold ash used as immune booster to children in southern India, *Indian Journal of Experimental Biology*, 2007;55(4), pp. 217-224

18. Rao P, Shailaja U., Mallika, K.J., Desai, S., Debnath, P., 2012, Traditional use of

Swarnamritprashan as a preventive medicine; Evidence based observational study in children, *IJRAP- International Journal of research in Ayurveda and pharmacy*, 2012;3[5]:Sept-Oct 2012

19. Sharma Sadananda, Rasatarangini, Ed. Shatri Kashinath, Motilal Banarasidas Publication, 11th Edition, Reprint 1989, verse 15/28, verse no 15/69, 15/71-80, PP 367, 375, 376.

20. Semmler-Behnke, M., Lipka, J., Wenk, A., Hirn, S., Schäffler, M., Tian, F., Schmid, G., Oberdörster, G., Kreyling, W.G., 2014, Size dependent translocation and foetal accumulation of gold nanoparticles from maternal blood in the rat., *Part Fibre Toxicol.* Sep 10;11:33. doi: 10.1186/s12989-014-0033-9.

21. Sharma Hariprapanna, Rasayogasagar II, 2nd edition, 1983, Krishnadas Academy, Choubhambha Press, Varanasi, India, PP 529, 530

22. Kulkarni DA, Rasaratnasamuchay, Ed. DA Kulkarni, Meharchand Lakshmandas Publications, 1942, New Delhi, India - gold bhasma, pp 92-96

23. Shastri Parshurama, Sharangdhar Samhita of Acharya Sharangdhar, Ed. Parshuram Shastri, Chauhambha Orientalia, 3rd edition, 1983, Varanasi, India, verse no- 4/13, 11/20, PP 242, PP 37.

24. Wijenayake A, Pitawala A, Bandara R, Abayasekara C, *J Ethnopharmacol.* 2014 Sep 11;155(2):1001-10. doi: 10.1016/j.jep.2014.06.051. Epub 2014 Jun 30. The role of herbometallic preparations in traditional medicine--a review on mica drug processing and pharmaceutical applications.

25. Pal D, Sahu CK, Haldar A., *J Adv Pharm Technol Res.* 2014 Jan; 5(1):4-12. doi: 10.4103/2231-4040.126980., Bhasma : The ancient Indian nanomedicine.

26. Borkar, Sartha Rasachandanshu, 3rd edition, 1905, Shrigajanan book depot, Dadar, Mumbai, , verse no. 453, verse no. 524-528, PP. 93, 413

27. Shah, N. C., Bharat Bhaishjya Ratnakar Vol 5, B. Jain Publishers, Reprint 1985, New Delhi, India, pp 415- 420, 421-422

28. Mishra Siddhinandan, [Translator], Rasaprakash Sudhakar of Acharya Yashodhar, 1983, First Edition, Choukhambha Orientalia, Varanasi, Chapter 4, pp 67-69

29. Yadav, K., Chaudhary, A. 2015, Percentage of Swarna Bhasma in medicaments of Ayurveda to treat disorders of different origin, *International Journal of Green Pharmacy*, 9(2), pp. 90-94, 2015

30. Shah, Z.A., Gilani, R.A., Sharma, P., Vohora, S.B., 2005, Attenuation of stress-elicited brain catecholamines, serotonin and plasma corticosterone levels by calcined gold preparations used in Indian system of medicine, *Basic and Clinical Pharmacology and Toxicology*, 96(6), pp. 469-474, 2005

31. Bajaj, S., Vohora, S.B., 2000, Anti-cataleptic, anti-anxiety and anti-depressant activity of gold

preparations used in Indian systems of medicine, *Indian Journal of Pharmacology* 32(6), pp. 339-346

32. Wiwanitkit V, Sereemasun A, Rojanathanes R., 2009, Effect of gold nanoparticles on spermatozoa: the first world report., *Fertil Steril.* 2009 Jan;91(1):e7-8. Epub 2007 Dec 11.

33. Jain V, Rai A, Misra S, Singh KM., 2010, Seminal gold content in healthy fertile men in India., *Int J Ayurveda Res.* 2010 Jul;1(3):172-4. doi: 10.4103/0974-7788.72490.

34. Shastri Lakshmi pati , Yogaratnakar, Uttarardha, Ed., *Chaukhambha Sanskrit Sansthan*, Sixth edition 1997, Varanasi, India, *Amlapittachikitsa*, Verse 5, PP 244

35. Pillai G., 2014, Nanomedicines for Cancer Therapy: An update of FDA approved and those under various stages of development. ,*SOJ Pharmacy and Pharmaceutical Sciences*, 6, 2014

36. Xia Q, Li H, Liu Y, Zhang S, Feng Q, Xiao K., 2017, The effect of particle size on the genotoxicity of gold nanoparticles., *J Biomed Mater Res A.* 2017 Mar;105(3):710-719. Epub 2016 Nov 7.

37. Alkilany, A.M. and Murphy, C. J. 2010, Toxicity and cellular uptake of gold nanoparticles: what we have learned so far?, *J Nanopart Res.* Sep; 12(7): 2313–2333. Published online 2010 Apr 6.

38. Kuppasamy, P, Yusoff, M. Y., Maniam G. P. , Govindan, N. , 2016, Biosynthesis of metallic nanoparticles using plant derivatives and their new avenues in pharmacological applications – An updated report , *Saudi Pharmaceutical Journal*, Volume 24, Issue 4, July 2016, Pages 473–484

39. Mukherjee S, Sau S., Durga M., Patra C., 2016, Green synthesis and characterization of monodispersed gold nanoparticles: Toxicity study, delivery of doxorubicin and its bio-distribution in

mouse model, *Journal of Biomedical Nanotechnology* 12(1):165-181 · January 2016

40. Mukherjee, S., Ghosh, S. Das, D.K., Chakraborty, P., Choudhury, S., Gupta, P., Adhikary A., Dey, S. , Chattopadhyay, S, 2015, Gold-conjugated green tea nanoparticles for enhanced anti-tumor activities and hepatoprotection — synthesis, characterization and in vitro evaluation, *The Journal of Nutritional Biochemistry*, Volume 26, Issue 11, November 2015, Pages 1283–1297

41. Katti, K., Chanda N., Shukla R. , Zambre A., Suibramanian T, Kulkarni R., Kannan R, Katti K., 2009, *Int J Green Nanotechnol Biomed.* 2009 Jan 1; 1(1): B39–B52. Doi: 10.1080/19430850902931599

42. Velusamy, P., Govindarajan, V.K., Venkadapathi, J., Das, J. and Pachaiappan, R., 2016, Bio-Inspired Green Nanoparticles: Synthesis, Mechanism, and Antibacterial Application. *Toxicological Research.* 2016;32(2):95-102. doi:10.5487/TR.2016.32.2.095.

43. Yadavji Trikamji [Editor], *Sushrutsamhita of Sushrut*, 4th edition, 1980, *Chikitsasthana* 28/14-24, *Choukhambha Orientalia*, Varanasi, India , PP 501, 502

44. Patil T. S. , Wele A. A, 2007, Significance of pharmacokinetics and pharmacodynamics of Piper nigrum L. [Marich] as an ingredient and possible marker of Ayurvedic formulations. *Indian Drugs.* 2007;44(5):329.

45. Soumen Das, Mangal C. Das, and Retina Paul, *Swarna Bhasma* in cancer: A prospective clinical study, *Ayu.* 2012 Jul-Sep; 33(3): 365–367. doi: 10.4103/0974-8520.108823

46. Paul W, Sharma CP, Deb KD. "Nature vs. nurture: gold perpetuates stemness"., *J Stem Cells.* 2011; 6(4):181-98.