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Efficacy of *Swarna-prash* in combating perinatal oxidative stress and its compatibility in newborns

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All neonates are exposed to a variable degree of oxidative stress that may result in cellular, tissue, or organ damage due to a low-efficient antioxidant system. The present study aimed to evaluate the effect of licked *Swarna-prash,* comprising 15 mg *Swarna-bhasma* (incinerated gold particles) mixed with 1 mL honey and 0.5 mL *Ghrita* (butter oil), given in perinatal oxidative stress. A randomized case-control study ensued after the microanalysis of InAuPs (Incinerated *Aurum* Particles) and *Swarna-prash*. Ninety newborns were registered, considering the inclusion and exclusion criteria, and divided into three groups.

The single dose of *Swarna-prash* was given once a day in Group A and thrice a day in Group B. Due to ethical issues, nothing was given except mother milk in Group - C (control group). Venous blood samples were collected from the umbilical cord after birth and 48 h for complete blood counts (CBC), Liver function test (LFT), Renal function tests (RFT), and antioxidant enzymes.

The *Swarna-bhasma* consisted of crystallite-size InAuPs ranging from 30.86 to 114.02 nm. The intergroup analysis of CBC, LFT, RFT, SOD, GSH, and catalase values shows in significant ($p>0.05$) variation except for the serum bilirubin and SOD in group-B v/s C, offers significant mean values ($p<0.05$). Finally, it can be inferred that *Swarna-prash* opposes neonatal perinatal oxidative stress, seems nontoxic, reduces the incidence of physiological jaundice, and is bio-compatible.

Keywords: Microanalysis, Newborns, Oxidative-stress, *Swarna-bhasma*, *Swarna-prash*

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Traditional, indigenous, or folk medicine existed before the emergence of modern medicine[1]. The traditional practice of *Swarna-prash,* a preparation of gold powder or incinerated *gold* particles mixed with *Madhu* (honey) and *Ghrita* (butter oil), has been imbibed in Indian culture since the *Vedic* period under the *Jatakarma Samskara*[2] and imparts *Medha* (intelligence) and *Ayu* (longevity) to the child. Further, recent studies (Fig. 1) reveal antimicrobial, anti-inflammatory, and antioxidant properties and impact on gut symbionts and pathobionts[3].

Ayurveda describes scientific methods to make metals bio-compatible[4] to humans and/or enhance bioavailability with the efficacy of the admixed substance. To avoid the toxicity of rubbed gold without purification, *Swarna-bhasma* (InAuPs)[5] was used as an ingredient of *Swarna-prash*.

Recent researches have shown antipseudomonal activity and antioxidant properties of all three components of *Swarna-prash*[6-10].

In-vivo studies[11-15] on *Swarna-bhasma* used with variable concentrations (57 wt % to 98 wt.6%) of elemental gold. The gold particles ranging from 2 to 25 µm and having 23 to 70 nm crystallite size have shown safe use in animal species for a maximum of 90 days in a variable dose (1 to 30 mg/kg body weight). *Suvarna bhasma* is not found to be genotoxic and mutagenic in a freshwater fish model at 3 mg and 30 mg/kg. *In vitro*, the cytotoxicity study[15] with a 28-35 nm crystallite size of the *Swarna-bhasma* did not cause blood cell aggregation or protein adsorption. In the mice model, *Swarna-bhasma* has shown enhanced activity of SOD and catalase activity.

Various studies have shown a breakdown of large-sized AuNPs or into smaller ones through different methods like trituration, sonification, or addition of the

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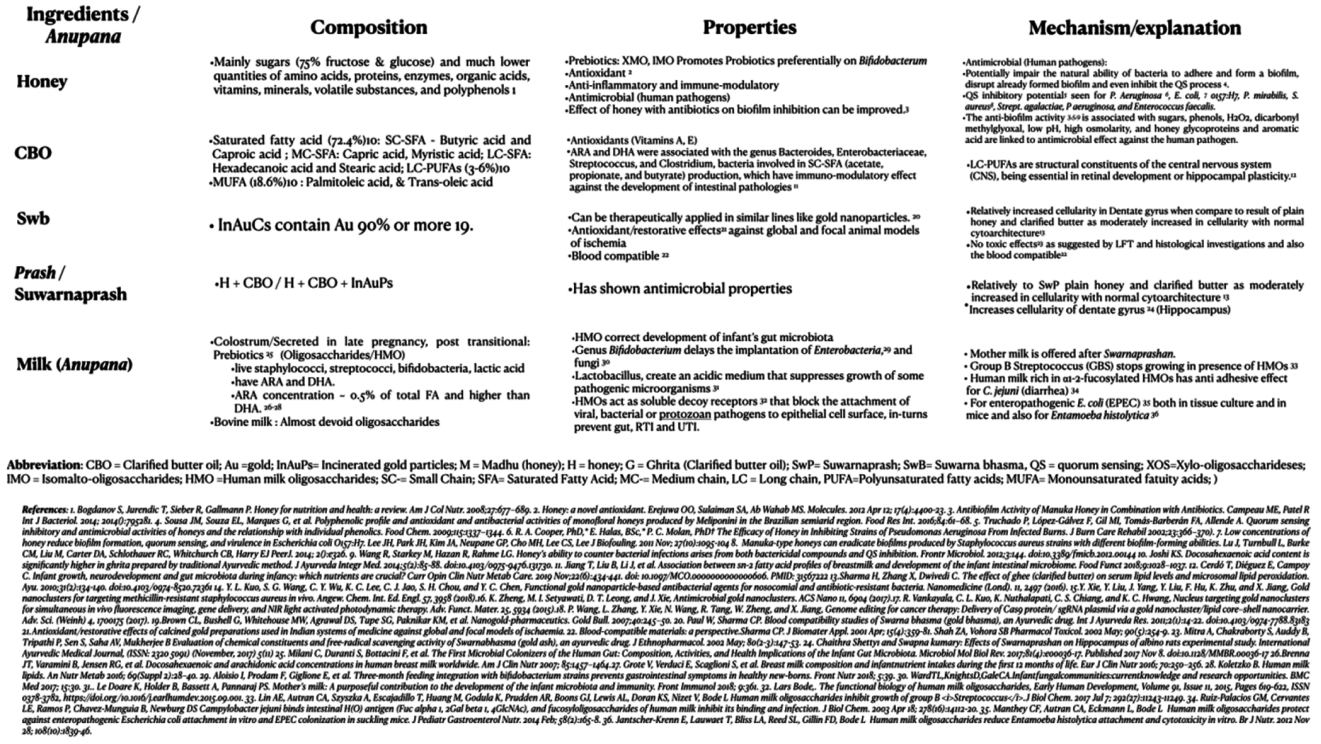

Abbreviation: CBO = Clarified butter oil; Au =gold; InAuPs= Incinerated gold particles; M = Madhu (honey); H = honey; G = Ghrita (Clarified butter oil); SwP= Suwarnaprash; SwB= Suwarna bhasma, QS = quorum sensing; XOS=Xylo-oligosaccharideses; IMO = Isomalto-oligosaccharides; HMO =Human milk oligosaccharides; SC-= Small Chain; SFA= Saturated Fatty Acid; MC-= Medium chain, LC = Long chain, PUFA=Polyunsaturated fatty acids; MUFA= Monounsaturated fatuity acids;)

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Fig. 1 — Research on *Prash*, *Swarna-prash* its ingredients and *Anupana* (~Drink after medication / ingestion)

honey (green synthesis of AuNPs)[16-19]. In contrast, by taking thin gold leaves triturated with purified *Parada* (processed Hg), and washed with Kanji (sour recipe), the *Swarna-bhasma* containing InAuPs is prepared through the thirteen *Putas* by adding pure sulfur[20]. As per the contemporary understanding, all neonates are exposed to a variable degree of oxidative stress irrespective of gestational period and mode of delivery. Nevertheless, a low-efficiency antioxidant system in the fetus and newborns cannot respond adequately to the harmful effects of free radicals, resulting in cellular, tissue, and organ damage[21]. The antioxidants form four lines of defense: preventive, radical scavenging, repair and de novo, and adaptation[22]. Superoxide dismutase, catalase, and glutathione peroxidase are categorized under preventative antioxidants as the first line of defence by suppressing the formation of free radicals. Superoxide dismutase catalyzes the breakdown of the superoxide anion into oxygen and hydrogen peroxide, while glutathione peroxidase and catalase reduce the hydrogen peroxide to water[23]. An imbalance between free radical production and antioxidant capacity is termed oxidative stress, and it may result in numerous disorders[24,25].

At birth, the newborn is exposed to a relatively hyperoxic environment[26] while the production of antioxidants is low due to the immaturity of antioxidant systems (both enzymatic and non-enzymatic)[27,28]. Hence, newborns are exposed to unavoidable oxidative stress during the transitional period, which results in increased prooxidative capacity in blood at least three days after birth[29]. Oxidative stress also reduces key antioxidants, including catalase, superoxide dismutase, glutathione, glutathione peroxidase, and glutathione reductase. An oral administration of *Swarna-bhasma* may reverse these enzymes in both focal and global ischemia models[30]. However, excessive formation of free radicals and inadequate production of antioxidants may cause free radical disease, *viz.,* Broncho-pulmonary dysplasia, PPHN, necrotising enterocolitis, periventricular leucoplasia, and retinopathy of prematurity[31].

Considering the antique references and emerging contemporary research on *Swarna-prash*, the present study was designed to evaluate the role of *Suwarna prash* in perinatal oxidative stress in newborns by assessing the antioxidant enzymes and their biocompatibility.

Materials and Methods

Study design, area, and period

The study was planned into two parts: first, physicochemical analysis of *Swarna-bhasma* through

the SEM (Scanning Electron Microscope), EDAX (Energy-dispersive X-ray analysis), and XRD (X-ray diffraction) while SEM and EDAX were performed for *Swarna-prash* to get the surface topography of InAuPs and the changes after blended with honey and butter oil. Second, the clinical research to evaluate the biocompatibility of *Swarna-prash* and its impact on perinatal oxidative stress by assessing CBC, LFT & RFT, and the antioxidant enzymes *viz.,* superoxide dismutase (SOD), glutathione reductase (GSH), and catalase (CAT).

Procurement of drugs

To prepare *Swarna-prash*, *Swarna-bhasma* was purchased from the market (Dabur Pvt Ltd*, Batch No. SB0232, Manufacturing Date - 12/17) for the physicochemical analysis and clinical study. *Madhu* (Dabur, Lot No. BM2539, manufacturing date - 09/18) and butter oil (*Britannia*, Lot No. 19B01A, manufacturing date-30/09/2018) were purchased from the market (GMP certified).

***Swarna-prash* preparation and administration**

After taking all the aseptic precautions, the recommended method[32] was used to prepare *Swarna-prash*. A freshly prepared *Swarna-prash* was administered to the newborn using the ring finger within ten minutes.

Microanalysis of samples

The samples were prepared for the microanalysis of *Swarna-bhasma* and *Swarna-prash,* which done by using SEM with EDAX and XRD. SEM was used to get good quality magnified images of dry and wet samples of *Swarna-bhasma* and *Swarna-prash*, respectively (Fig. 2 a & b), at a specific WD (working distance), voltage and by using the ETD (Everhart–Thornley detector), LFD (Large Field Detector) and GSED (Gaseous secondary electron detector).

Scanning electron microscopic (SEM), EDAX and X-ray diffraction

Images of *Swarna-bhasma* and *Swarna-prash* were acquired using SEM (Quanta 200F) with energy dispersive x-ray analysis using LFD and GSED, respectively. X-ray diffraction of the sample was carried out on a Malvern Panalytical's X-ray Diffractometer.

Clinical study design

A total of 90 full-term, appropriate for gestational age (AGA) newborns were registered from the institution's neonatal care unit after getting informed written consent from their parents. We excluded the case if their mother had any systemic acute or chronic illness during the antenatal period or was on the drug (s) known to pose a risk to the fetus. Any neonate requiring resuscitation or having congenital/hereditary

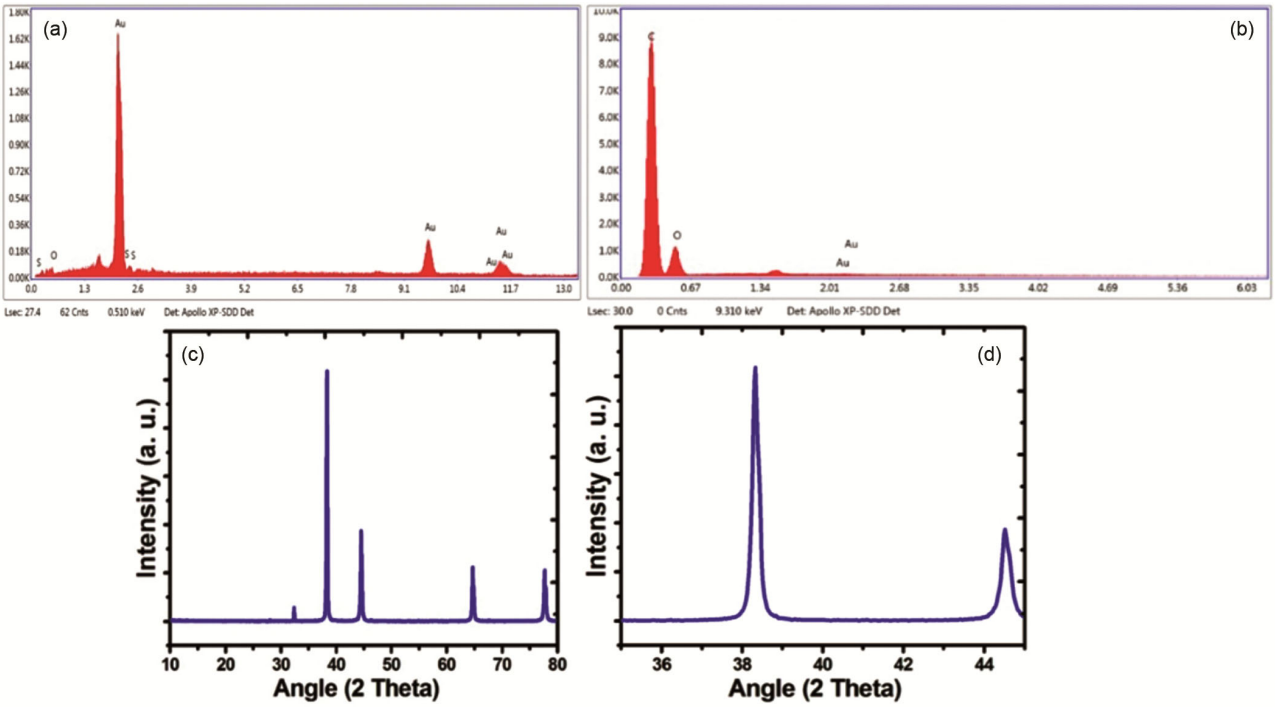

Fig. 2 — (a) EDX imaging shows the elemental composition of *Swarna-bhasma*, (b) EDX imaging shows the elemental composition of *Swarna-prash,* (c) Graph shows the XRD pattern of *Swarna bhasma*, (d) Graph shows a closer view of the XRD peaks

disorders was also excluded. There was no drop-out during the study period. These cases were further divided randomly by adopting a stratified sampling method (computer-generated randomization) into three groups. Group A (n=30): The child received a *single dose of Swarna-prash* on the first day; Group B (n=30): The child received *Swarna-prash* three times on the first day, and Group–C (n=30): no medication was given except the mother feeding. All the groups were kept under observation from day 1 to day 3.

The study was approved by the Institute Ethical Committee and registered with CTRI (Registration Number- CTRI/2018/04/013513).

Dose determination

In humans, the recommended therapeutic dose of *Swarna-bhasma* ranges from 1/8th to 8 Ratti[33,34] (15 mg to 960 mg). After considering the wide margin of safety in animals and humans[35,36], 15 mg dose of *Swarna-bhasma* was considered. The recommended dose of *Ghrita* for a newborn child is equal to one *Kolasthi* (~ 500 mg or 0.5 mL/dose). An equal amount of honey and *Ghrita* is antagonistic and is contraindicated for human use[37]. Therefore, to avoid antagonistic effect, an unequal amount of *Madhu* (1.0 mL/dose) and *Sarpis* was given.

Sample collection

After delivery, cord blood was collected for routine investigations and taken to the concerned laboratory to assess markers for oxidative stress, *i.e.,* SOD, CAT, and GSH. After 48 h, blood was collected from the newborns and sent to the laboratory to evaluate free radical levels and renal and liver integrity in newborns after *Swarna-prash*.

Morbidity assessment was made through clinical evaluation on the first follow-up of the seventh day of life.

Analytical method for the oxidative enzymes

Cord blood at birth and venous blood after 48 h were collected in different vials containing Ethylene Diamine Tetracetic Acid (EDTA) as an anticoagulant. Ten microliters of blood were diluted 100 times and stored at -20°C until analysis. Estimation of SOD activity was done using the method of *McCord* and *Fridovich*, CAT activity was determined according to *Aebi's* method, and estimation of GSH content was done using *Ellman's* method.

Statistical analysis

The *t*-test and one-way ANOVA with post-hoc test were used for statistical analysis to compare the levels of antioxidant enzymes, CBC, LFT, and RFT at birth and after 48 h.

Results

Physicochemical characterization:

Based on the SEM results, the *Swarna-bhasma* contains agglomerated spherical-shaped gold particles of ~2 to 3 μm in size with a porous surface. The EDX results showed the presence of 95.1% wt%, Au in the *Swarna-bhasma*, while 0.02 wt% Au in *Swarna-prash*. The carbon in *Swarna-bhasma* is 0.7 wt%, while *Swarna-prash* has 82.63 wt%. Oxygen concentrations are also reflected in Figure 2 a & b and Table 1. The SEM images captured using GSED, show multiple elevated InAuPs embedded into a rippled *Prash* (honey + butter oil) matrix, visible gaseous bubble, and disintegrated micro-sized InAuPs. (Fig. 3 c & d).

The XRD pattern of *Swarna-bhasma* shows sharp peaks (Fig. 2 c & d), indexed as crystalline gold JCPDS, USA. The crystallite size of InAuPs was calculated through the online 'XRD crystallite size calculator,' and it ranges from 30.83 to 114.02 nm.

Clinical study

Out of ninety registered full-term newborns, 52.3% and 47.7% were males and females, respectively. Regarding the mode of delivery, 18.9% of cases were delivered via spontaneous vaginal delivery with vertex presentation and 81.1% of cases by elective lower segment caesarean section (LSCS) in healthy mothers.

Assessment parameters for blood compatibility and non-toxicity of Swarna-prash

Complete blood count (*CBC*)

On intragroup comparison, the mean difference values of haemoglobin, TLC, RBC, and platelets are

Table 1 — Major elemental composition of *Swarnabhasma* and *Swarna-prash* by EDAX (Weight %)

Element	*Swarna-bhasma* (*Sample -I*)	*Swarna-prash* (*Sample-II*)
C/S*	0.7*	82.63
O	4.2	17.35
Au	95.1	0.02

*The Sulphur was detected in *Swarna-bhasma* (Sample-1) and 'C' (Carbon) in *Swarna-prash* (Sample-2).

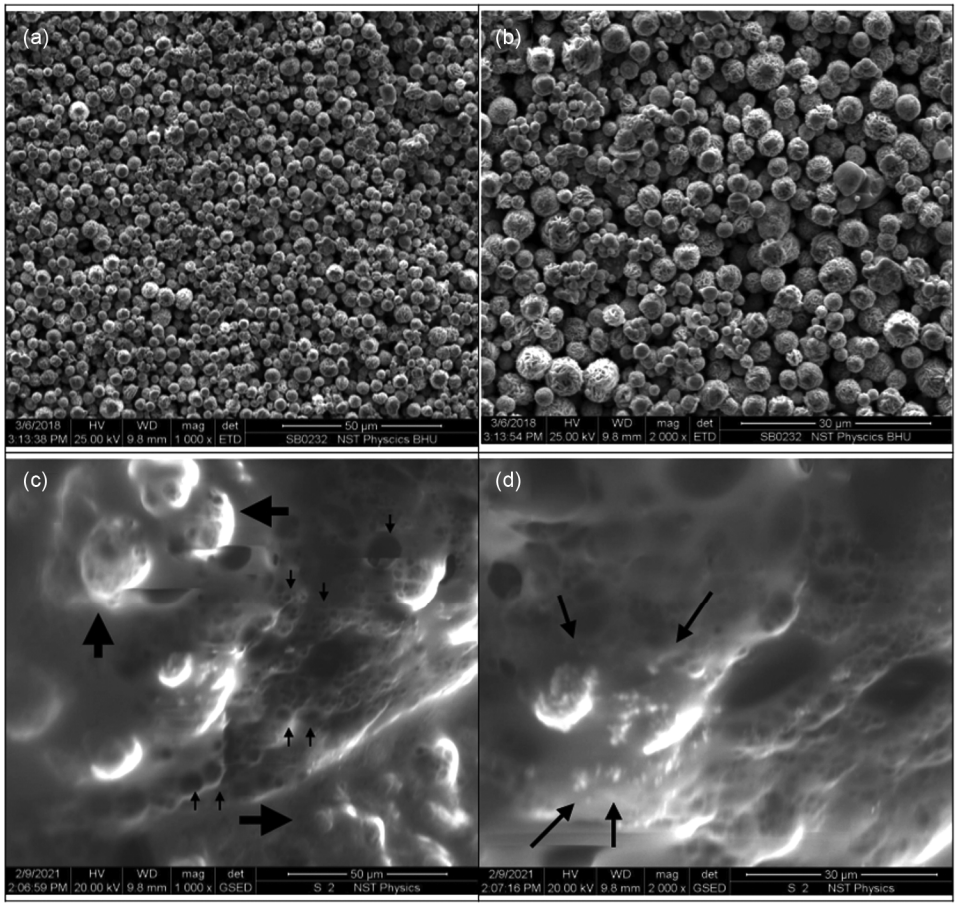

Fig. 3 — SEM images captured using ETD & GSED with a WD 9.8 mm (a) SEM image of dry InAuPs using ETD (1000x magnification, 25Kv; at 50 μm scale bar) (b) SEM image using ETD (2000x magnification, 25Kv; at 30 μm scale bar) (c) SEM image using GSED, showing the multiple elevated InAuPs embedded (large lack arrow) into rippled Prash (honey + CBO) matrix showing incinerated spherical gold particles under process (releasing the gaseous bubble-thin small arrow) (1000x magnification. 20 Kv, at 50 μm scale bar) (d) SEM image using GSED showing disintegration (black arrow) of micro-sized InAuPs (2000x magnification. 20 kV: at 30 μm scale bar)

found to be statistically significant ($p<0.05$) in all groups but seen as insignificant ($p>0.05$) on the intergroup comparison. The mean difference in Neutrophil, Lymphocyte, Monocyte, and Eosinophil values was found to be statistically insignificant ($p>0.05$) on inter/intragroup comparison. (Table 2).

Liver function tests (*LFT*)

The mean difference values of serum glutamic oxaloacetic transaminase (SGOT), serum glutamic pyruvic transaminase (SGPT), direct serum bilirubin, serum protein, and albumin were statistically insignificant ($p>0.05$) on the intergroup comparison, while statistically significant ($p<0.05$) in all groups on the intragroup comparison. The mean-difference value of alkaline phosphatase (ALP) was also found to be statistically insignificant ($p>0.05$) in the intergroup comparison. In all groups, the mean difference in total serum bilirubin is statistically significant ($p<0.05$) in the intergroup and intragroup comparisons; however, the mean difference in group C was higher than that of group B when compared between A v/s C and B v/s C (Table 2).

Renal function tests (*RFT*)

The mean difference in serum creatinine was lower in group A compared to groups B and C. The mean difference of blood urea, serum sodium, potassium, and chloride was found to be statistically insignificant ($p>0.05$) on the intergroup comparison (Table 2).

Assessment of the antioxidative effect of Swarna-prash

The mean difference for SOD values in the intergroup comparison is seen as significant ($p<0.05$) and relatively higher in group B. (Table 3). These findings suggest a better antioxidant effect of *Swarna-prash* when given three doses on the first day than the single dose on the first day to newborns.

Table 2 — Intragroup and intergroup comparison of different components of C.B.C., LFT, and RFT in various groups: at registration (R) v/s after 48 h, n=90

Group (N=90, n=30 in each group)	Mean difference±S.D.	Paired t	p-value
Hb (g/dL): Intragroup comparison			
A	1.43±1.439	5.466	0.000
B	1.89±1.347	7.686	0.000
C	1.94±1.692	6.266	0.000
Between-group comparison one-way ANOVA	F= 1.054 p= 0.352		
TLC (/mm^3): Intragroup comparison			
A	2079.16±2221.266	5.466	0.000
B	1959.80±924.866	7.686	0.000
C	1327.00±2167.696	3.353	0.002
Between-group comparison one-way ANOVA	F= 1.4022 p= 0.2516		
Neutrophil (%): Intragroup comparison			
A	0.06±10.967	0.033	0.974
B	1.23±12.819	5.27	0.602
C	0.80±14.291	0.307	0.761
Between-group comparison one-way ANOVA	F= 10.5070 p= 0.0645		
Lymphocytes (%): Intragroup comparison			
A	0.90±11.186	0.441	0.663
B	4.30±14.300	1.647	0.110
C	3.36±14.968	1.232	0.228
Between-group comparison one-way ANOVA	F= 0.5011 p= 0.6076		
Monocytes (%): Intragroup comparison			
A	1.00±5.988	0.915	0.368
B	0.97±3.528	1.501	0.144
C	2.067±6.384	1.773	0.087
Between-group comparison one-way ANOVA	F= 0.3946 p= 0.6752		
Eosinophils (%): Intragroup comparison			
A	0.50±2.080	1.316	0.198
B	0.10±1.959	0.275	0.785
C	0.26±2.333	0.626	0.536
Between-group comparison one-way ANOVA	F= 0.9560 p= 0.3884		
Basophils (%): Intragroup comparison			
A	0.33±0.669	0.273	0.787
B	0.17±0.950	0.961	0.344
C	0.23±0.774	1.651	0.109
Between-group comparison one-way ANOVA	F= 3.8417 p= 0.0252 A v/s B: p= 0.7231 A v/s C: p= 0.0230 B v/s C: p= 0.1386		

… *Contd.*

Table 2 — Intragroup and intergroup comparison of different components of C.B.C., LFT, and RFT in various groups: at registration (R) v/s after 48 h, n=90 (Contd.)

RBC (millions/mm^3): Intragroup comparison

Group	Mean difference±S.D.	Paired t	p-value
A	0.55±0.567	5.342	0.000
B	0.77±0.806	5.259	0.000
C	0.85±0.738	6.322	0.000
Between-group comparison one-way ANOVA	F= 1.4329 p= 0.2442		

Platelets (lakhs/mm^3): Intragroup comparison

Group	Mean difference±S.D.	Paired t	p-value
A	0.37±0.704	2.881	0.007
B	0.30±0.818	3.550	0.001
C	0.45±0.743	3.373	0.002
Between-group comparison one-way ANOVA	F= 0.2953 p= 0.7450		

SGOT (U/L): Intragroup comparison

Group	Mean difference±S.D.	Paired t	p-value
A	14.77±17.491	4.627	0.000
B	10.38±14.856	3.828	0.001
C	17.48±12.385	7.733	0.000
Between-group comparison one-way ANOVA	F= 1.6990 p= 0.189		

SGPT (U/L): Intragroup comparison

Group	Mean difference±S.D.	Paired t	p-value
A	6.57±10.377	3.471	0.002
B	9.62±14.419	3.657	0.001
C	7.07±7.243	5.351	0.000
Between-group comparison one-way ANOVA	F= 0.654 p= 0.522		

ALP (U/L): Intragroup comparison

Group	Mean difference±S.D.	Paired t	p-value
A	39.99±37.671	5.815	0.000
B	15.56±72.444	1.177	0.249
C	33.66±63.442	2.907	0.007
Between-group comparison one-way ANOVA	F= 1.353 p= 0.264		

Total Serum bilirubin (mg/dL): Intragroup comparison

Group	Mean difference±S.D.	Paired t	p-value
A	6.37±3.248	10.747	0.000
B	6.24±2.951	11.582	0.000
C	8.26±3.484	12.999	0.000
Between-group comparison one-way ANOVA	F= 3.6642 p= 0.029 A v/s B: p= 0.986 A v/s C: p= 0.066 B v/s C: p= 0.046		

Direct Serum bilirubin (mg/dL): Intragroup comparison

Group	Mean difference±S.D.	Paired t	p-value
A	0.16±0.214	4.219	0.000
B	0.15±0.244	3.367	0.002
C	0.20±0.231	4.772	0.000
Between-group comparison one-way ANOVA	F= 0.397 p= 0.674		

Serum protein (g/dL): Intragroup comparison

Group	Mean difference±S.D.	Paired t	p-value
A	1.26±0.451	15.320	0.000
B	1.09±0.897	6.661	0.000
C	1.19±0.705	9.285	0.000
Between-group comparison one-way ANOVA	F= 0.436, p= 0.647		

… Contd.

Table 2 — Intragroup and intergroup comparison of different components of C.B.C., LFT, and RFT in various groups: at registration (R) v/s after 48 h, n=90 (Contd.)

Serum albumin (g/dL): Intragroup comparison at registration v/s after 48 hours			
Group	Mean difference±S.D.	Paired t	p-value
A	0.77±0.469	8.996	0.000
B	0.54±0.565	5.198	0.000
C	0.48±0.380	6.931	0.000
Between-group comparison one-way ANOVA	F= 3.085 p= 0.050 A v/s B: p= 0.154 A v/s C: p= 0.054 B v/s C: p= 0.878		
Serum creatinine (mg/dL): Intragroup comparison			
Group	Mean difference±S.D.	Paired t	p-value
A	0.11±0.185	3.391	0.002
B	0.23±0.173	7.575	0.000
C	0.23±0.169	7.478	0.000
Between-group comparison one-way ANOVA And Post Hoc Test	F= 4.6594 p= 0.0120 A v/s B: p= 0.0261 A v/s C: p= 0.0261 B v/s C: p= Not a Number		
Blood urea (mg/dL): Intragroup comparison			
Group	Mean difference±S.D.	Paired t	p-value
A	6.08±7.180	4.638	0.000
B	3.86±6.830	3.095	0.004
C	6.31±8.149	4.239	0.000
Between-group comparison one-way ANOVA	F= 1.0009 p= 0.3717		
Serum sodium (mmol/L): Intragroup comparison			
Group	Mean difference±S.D.	Paired t	p-value
A	4.03±4.996	4.422	0.000
B	3.36±5.402	3.407	0.002
C	5.51±4.029	7.494	0.000
Between-group comparison one-way ANOVA	F= 1.5478 p= 0.2185		
Serum potassium (mmol/L): Intragroup comparison			
Group	Mean difference±S.D.	Paired t	p-value
A	0.83±1.899	2.398	0.023
B	0.73±1.921	2.077	0.047
C	0.94±1.651	3.257	0.003
Between-group comparison one-way ANOVA	F= 0.0991 p= 0.9058		
Serum chloride (mmol/L): Intragroup comparison			
Group	Mean difference±S.D.	Paired t	p-value
A	2.08±4.842	2.353	0.026
B	2.26±5.641	2.197	0.036
C	2.58±4.338	3.257	0.003
Between-group comparison one-way ANOVA	F= 0.0779 p= 0.9251		

Assessment of morbidity

The incidence of neonatal jaundice was seen as higher in group C than in groups A and B. No specific variation was seen in the incidence of other problems on the first follow-up (Table 4).

Discussion

The XRD pattern of *Swarna-bhasma* was similar to JCPDS data no: 01- 1174, which confirms that *Swarna-bhasma* comprises pure gold. The XRD analysis of *Swarna-bhasma* shows 65 nm, an average size of InAuPs. The further reduction of size is supported by the SEM image representing the disintegration. (Fig. 3 c & d) This size reduction may be attributed to the trituration of *Swarna-bhasma* with honey and *Ghrita* (butter oil) as occurs in a past study[38],

Table 3 — Intergroup comparison of S.O.D., C.A.T. and G.S.H. values in various groups:

	SOD		
Group	Mean difference±S.D. (U/mg Hb)	Paired t	p-value
A	0.132±0.123	6.102	0.000
B	0.221±0.106	12.867	0.000
C	0.126±0.079	8.736	0.000
Between-group comparison one-way ANOVA	F= 7.8124 p= 0.0008 (<0.001)		
Post Hoc Test	A v/s B: p=0.0039 (Diff=0.0890, 95% CI=0.0248 to 0.1532)		
	A v/s C: p=0.9730 (Diff=-0.0060, 95%CI=-0.0702 to 0.0582)		
	B v/s C: p=0.0019 (Diff=-0.0950, 95%CI=-0.1592 to -0.0308)		
	Catalase		
Group	Mean difference±S.D. (U/mg Hb)	Paired t	p-value
A	0.223±0.122	10.003	0.000
B	0.233±0.106	12.042	0.000
C	0.170±0.155	5.980	0.000
Between-group comparison one-way ANOVA	F= 2.057 p= 0.134		
	GSH		
Group	Mean difference±S.D. (µg/mg Hb)	Paired t	p-value
A	0.950±0.462	11.240	0.000
B	1.016±0.294	18.913	0.000
C	0.773±0.667	6.351	0.000
Between-group comparison one-way ANOVA	F= 1.908 p= 0.154		

Table 4 — Incidence of ailments aroused during the hospital stay

COMPLAINTS	GROUP A	GROUP B	GROUP C
Eye discharge (watery)	1 3.33%	2 6.66%	3 10.0%
Maculopapular rashes	2 6.66%	3 10.0%	1 3.33%
Pustular rashes (pyoderma)	1 3.33%	2 6.66%	1 3.33%
Regurgitation (curdy)	0	1 3.33%	1 3.33%
Increased frequency of loose stool (Other stool characteristics were normal)	1 3.33%	1 3.33%	1 3.33%
Umbilical Discharge (mucopurulent)	0	0	1 3.33%
Yellowish discoloration of the skin (Physiological jaundice)	18 60.00%	17 56.67%	26 86.67%
Peeling of skin	2 6.66%	2 6.66%	0 (00)

wherein relatively smaller nanosized gold particles were formed.

The current study analyzed the changes in oxidative stress biomarkers, *i.e.,* S.O.D., C.A.T., and G.S.H., which influence postnatal changes in newborns in the first 48 h. In addition, the present study surfaced insignificant variation in C.B.C., LFT, and RFT on the intergroup comparison after 48 h of *Swarna-prash* administration, which favors its bio-compatibility (Table 2)[39].

Despite significant mean difference values in SGOT, SGPT, and ALP (p<.001) at 48 h after birth, there was no significant variation in both treated groups from the control (p=0.189) when one-way ANOVA was applied. No alteration in LFT and RFT values is observed after 48 h of *Swarna-prash* administration, which signifies its non-toxic effect on hepatocytes and nephrons. The LFT and RFT support the hepatic and renal integrity (Table 2).

Physiological jaundice in newborns starts appearing after 48 h. The mean serum level of bilirubin was not beyond the physiological range in any group (Table 2). However, the mean difference value of total serum bilirubin (mg/dL) of groups A and B was observed lower (6.37±3.248 mg/dL & 6.24±2.95 mg/dL) than that of Group C (8.26±3.48 mg/dL). However, the physiological concentration of bilirubin protects neonatal red blood cells against oxidative stress[40], and in the present study, the level of serum bilirubin was observed to be relatively lower in newborns of groups A & B. It might be due to the antitoxic effect of increased activity of SOD against the production of superoxide generation. Hence, protective elevated levels of SOD in Group A and Group B may subdue the production of Serum bilirubin.

The mechanism for the antioxidant effect of *Swarna-prash* in newborns may be better understood by the above study. *Swarna-bhasma* has crystallite-size gold nanoparticles ranging from 30.83 to 114.02 (nm), and during the *Swarna-prash* preparation, these particles get disintegrated into smaller particles (Fig. 3 a-d). InAuPs in *Swarna-prash* are partially absorbed sublingually through transcytosis and into the cells mainly by macro-pinocytosis and clathrin-dependent receptor-mediated endocytosis in HeLa (human cells derived from cervical cancer) and HFF-1 (human foreskin fibroblast cells) without causing any toxic effect[41,42]. InAuPs may eventually enhance the intracellular concentration of the SOD, as suggested by higher values of SOD in neonates of group B compared to control group C in the present study (Table 3).

Previous studies have shown that increased activity of SOD is an important antioxidant enzyme having an antitoxic effect against superoxide anion and results in increased dismutation of superoxide to hydrogen peroxide. The potential antioxidant activity of *Swarna-bhasma,* an ingredient of *Swarna-prash,* has been supported by in-vivo animal studies[5,6] on mice and on albino rats model and has resulted in a significant rise of SOD and catalase activity, in turn, effectively reduces free radical concentrations.

Madhu (honey), one of the components of *Swarna-prash*, might exert an additional hepatoprotective effect due to its potentiating or *Yogavahi* effect[43]. Further, the presence of vitamins A and E in the *Ghee* (clarified butter oil) has an antioxidant effect and can reduce oxidative injury[5] and might contribute to reducing oxidative stress in neonates.

Conclusion

Swarna-prash is bio-compatible and non-toxic to the liver and kidneys. Three dosages of *Swarna-prash* (15 mg/dose) on the first day of life have a role in defying perinatal oxidative stress in healthy neonates by enhancing the SOD activity and reducing the incidence of physiological jaundice clinically without causing significant reno-hepatic enzyme alteration.

Further, a dose-ranging experimental and clinical study is warranted to get the optimum dose of InAuPs for combating perinatal oxidative stress without altering its longevity and intellect-enhancing qualities.

Limitations and further scope of the study

It is challenging to draw robust conclusions due to the vulnerable population, diversity, small sample size, and short duration. The manifestation of disorders resulting from perinatal oxidative stress may take time to manifest. Future research can focus on oxidative stress-related disorders and the long-term effect of *Swarna prashana* in newborns. Expanding the research to include a more diverse neonatal population will improve the generalizability of the findings. Exploring optimal dosages and administration regimens for *Swarna prashana* in neonates, ensuring safety and efficacy while minimizing potential risks, and incorporating *Suwarna prash* in the routine care of newborns are avenues for further investigation. Study results may be further substantiated in mammalian animal models. Histo-pathology studies are warranted for assessing the hepatic and renal cytoarchitectural changes.

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Conflict of Interest

The authors declare no conflicts of interest associated with this manuscript.

Author Contributions

SS, BMS, and YBT were involved in conceptualization, study designing, methodology, formal analysis, clinical study, and investigations. Further, SS and KS were also engaged in the microanalysis of *Swarna-bhasma* and *Swarna-prash* through the SEM, EDAX, & XRD in the Lab of Late Prof. O.N. Srivastava Lab, Department of Physics, B.H.U. SS analysed the antioxidant enzyme in the Medicinal chemistry lab under the supervision of YBT. BMS is the communicating author who provides the concept of the work and overviews the whole research work.

Ethics Approval

The institute ethical committee (Dean/2018/EC/298, IMS) approved the study and registered with CTRI (Registration number CTRI/2018/04/013513).

Informed Consent

Informed consent was obtained from the parents of neonates who participated in the study.

Data Availability

The data are exclusively retained by the authors.

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