



Review Article

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THANGA URAM: A DUAL PERSPECTIVE REVIEW OF ITS PHARMACOLOGICAL BENEFITS IN MODERN AND SIDDHA MEDICINE

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ABSTRACT

The Siddha system of medicine uses mineral and metallic compounds for their high bioavailability and efficacy at low doses. Thanga uram (TU) is one such Siddha Metallo-mineral formulation. A review of the scientific literature on the ingredients of Thanga uram (TU) was undertaken. This wide-ranging assessment involved searching through Siddha literature as well as relevant publications in multiple databases and electronic search engines, including Google scholar, Embase, Mendeley, Pub Med Central, Science Direct, and the National Library of Medicine (NLM). The aim was to gather all pertinent information available on the subject. Thanga uram, with its validated antimicrobial, spermatogenic, cognitive enhancement, and styptic properties, and favourable safety profile, stands as a promising Siddha formulation. Its blend of traditional knowledge and scientific validation underscores its potential in contemporary medicine. The pharmacological actions and organoleptic characteristics of the substance align closely with the indications cited in the literature. This congruence suggests that the substance can be effectively utilized in the treatment of various diseases. Its efficacy is supported by both traditional use and modern scientific validation, making it a promising option for therapeutic applications

Keywords: Thanga uram, genito-urinary diseases, cognitive enhancement.

INTRODUCTION

The Siddha system of medicine is an ancient traditional healing practice that has been used for centuries in India. It employs a diverse range of mineral and metallic compounds in its formulations, which are believed to offer potent therapeutic benefits. These compounds are often used in lower doses but are known for their high bioavailability, meaning they are readily absorbed and utilized by the body ¹. The metallic/mineral formulations are believed to offer potent therapeutic benefits including rejuvenation, enhanced immunity, and treatment of chronic ailments ². The metals and minerals are converted to parpam, chenduram, Chunnam, pathangam etc. Prior to formulating a medicine, each ingredient is purified meticulously to minimize toxicity and enhance efficacy. Parpam, chenduram, Chunnam, pathangam which consists of mineral and metallic oxides, sulphides, caustic oxides, sublimes is known for its remarkable shelf life, retaining its potency for up to 100, 75, 500, 10 years respectively ^{3,4}. Parpam is the oxidized form of metal and mineral which are prepared by various procedures. One such formulation is TU, which is a metallo-mineral preparation widely used in Siddha medicine. It is indicated for various conditions, including male and female genito-urinary disorders, chronic

leucorrhoea (a vaginal discharge), venereal diseases, and as a tonic to enhance appetite and memory power ^{4,5}. According to Siddha literature Uram meaning Thangam (gold) or parpam (Calcinated powder) ⁶. However, despite its historical use and anecdotal evidence of efficacy, the globalization of Siddha medicine has been hindered by the lack of scientific evidence supporting the use of these compounds. In recent years, there has been a shift towards evaluating traditional medicines, including Siddha formulations, through scientific scrutiny to establish their efficacy and safety. With the increasing preference for natural products over chemically synthesized pharmaceuticals, there is a renewed interest in mineral-based medicines like TU. These formulations highlight the unique approach of Siddha medicine in integrating minerals and metals into therapeutic practices, following ancient protocols to harness their benefits while minimizing risks. Research into the pharmacological properties, mechanisms of action, and safety profiles of these formulations is crucial for their acceptance and integration into modern healthcare practices. As such, ongoing scientific investigations are shedding light on the potential benefits of Siddha medicines and may pave the way for their wider acceptance and use globally ².

LITERATURE REVIEW

Table 1: Drug Profile of Thanga Uram

Ingredient	Tamil name	Taste	Potency	Divison	Action
Mercury	Rasam	Inippu (Sweet), Pulippu (Sour), Uppu (Salt), Kaarppu (Spicy), Kaippu (Bitter), Thuvvarppu (Astringent)	Veppam & Thatppam	Based on with what it reacts	Alterative, Tonic, Laxative, Diuretic, Antiseptic ⁴
Sulphur	Gandhagam	Kaippu (Bitter), Thuvvarppu (Astringent)	Veppam	Kaarppu	Alterative, Antiseptic, Laxative, Diuretic ⁴
Stannum (Tin)	Velvangam	Kaippu (Bitter)	Veppam	Kaarppu	Astringent, De-obstruent, Antiseptic, Sedative ⁴
Ammonii chloridum	Navaacharam	Kaippu (Bitter), Pulippu (Sour)	Veppam	Kaarppu	Expectorant, Diuretic, Anti bilious, Diaphoretic ⁴
Nitric acid	Vediuppu dravagam	-	-	-	Coolant, Diuretic, Tonic ⁴

PURIFICATION

Mercury

1. Grind Rasam (Mercury) with Turmeric (*Curcuma longa* Linn) and Brick powder for 1 hour, then burn with *Acalypha indica* Linn leaf juice till evaporates^{4,7}.
2. A thick cloth (Kambili) is used to squeeze the needed quantity of mercury 1000 times. After that, it is put in an earthen pot and fresh water is added and heated. More water is added to maintain the water level. Mercury gets separated from the water when it turns black^{4,7}.
3. After extracting the chilly seeds (*Capsicum annum* Linn) mercury is placed inside. Ivy gourd (*Coccinia grandis* Linn) leaf poultice of four fingers thickness is applied to the chiles, wrapped with seven layers of mud-paste-coated fabric, dried, and calcinated with ten cow dung cakes (Kukkuda pudam)^{4,7}.

Sulphur

1. Combine the paste made from *Lawsonia inermis* Linn leaves with cow's curd in a mud pot; cover it with another pitted pot; add sulfur to the top and seal it with another mud pot; bury it in a hole; add cow dung cakes on top of the mud; burn it until the sulfur melts and descends; collect and repeat this process seven times⁴.
2. Melt sulfur with butter from cows and pour it into cow's milk; take the resulting sulfur and pour it in a mud pot; repeat this process thirty times; each time using fresh milk⁴.
3. Instead of milk, sulphur is melted ten times in banana stem juice (*Musa paradisiaca* Linn). This method is done for 10 times. By this method, it is said that the oil in the sulphur will be removed⁴.

Tin

1. Tin is powdered and soaked in 210 g of plant juice of iveli (*Diplocyclos palmatus* Linn) and isolated for a day and washed. Then the process is repeated for 9 more days washed and isolated without juice for 2 days. The same procedure should be repeated for one more time. Then 5.3l of juice is

taken in a earthen pot sealed using mud pasted cloth and buried for 20 days⁴.

2. Tin is melted and poured in a pot containing goat's urine, gingelly oil and juice of Pirandai (*Cissus quadrangularis* Linn). It is then allowed to cool⁴.
3. Tin is melted and poured to a mixture of turmeric (*Curcuma longa* Linn) and the juice of notchi (*Vitex negundo* Linn). The process is repeated twice and purified tin is obtained⁴.
4. Powdered tin is soaked in juice of *Vitex negundo* Linn and isolated until dry⁴.
5. Stool of bandicoot can also be used to purify tin⁴.

Preparation: The preparation of TU involves grinding purified ingredients with Nitric acid until the consistency of Mezhugu (wax) is achieved. The mixture is then subjected to controlled burning for 25 hours before cooling^{4,5}.

Indications and Dosage: TU is indicated for various male and female urogenital disorders, chronic leucorrhoea, venereal diseases, and as a tonic. The recommended dosage ranges from 130mg to 260mg^{3,5}.

LITERATURE REVIEW OF INGREDIENTS

Mercury: Mercury is the only metal in liquid form having the atomic number 80⁸. It is a transition metal. It has been widely used in biomedical applications. Traditionally, it is widely used in the treatment of syphilis⁹.

Sulphur: Sulphur (S) has an atomic number 16. It is a non-metal¹⁰. It is the 5th most abundant metal on the earth and it occurs as sulphide or sulphate mineral in nature^{11,12}.

Tin: Tin (Sn) has an atomic number 50. It is a post transition metal meaning it can exhibit both the properties of metals and non-metals. It is soft, malleable, ductile and corrosion resistant¹³. Previous study states that, tin plays a vital role in functions of adrenal gland. Tin in association with adrenal gland controls the left side of ventricle. Thus, low level of vitamin B1, C and Tin can lead to cardiac insufficiency¹⁴.

Table 2: Pharmacological action of ingredients in TU

Ingredient	Activity	Reference
Mercury and Mercurial Salts	Antibacterial	For more than 3,000 years, mercury and its derivatives have been utilized for various purposes including as anti-parasitic, anti-syphilis, antipruritic, preservative, anti-inflammatory, diuretic, anti-bacterial agents, in dental amalgams as substitutes ⁹ .
	Anti-inflammatory	
	Anti-apoptosis	
Sulphur	Anti-bacterial	Choudhury, Roy et al. (2012) reported significant antibacterial activity of polyethylene glycol-stabilized SNP against multidrug-resistant bacteria including <i>E. coli</i> , <i>Klebsiella pneumoniae</i> , <i>Acinetobacter baumannii</i> , <i>Stenotrophomonas maltophilia</i> , and <i>Enterobacter aerogenes</i> using agar dilution and broth microdilution methods. The study indicated a minimum inhibitory concentration (MIC) of 18.82 µg/mL for SNPs against all tested organisms ¹⁵ .

	Anti-fungal	Choudhury et al. (2011) synthesized surface-modified silver nanoparticles (SNPs) using a modified liquid-phase precipitation method. They employed sodium polysulfide and ammonium polysulfide as starting materials, with polyethylene glycol-400 (PEG-400) serving as the surface stabilizing agent. The researchers investigated the antifungal properties of these SNPs against the food spoilage fungi <i>Aspergillus niger</i> , which commonly contaminates fruits, vegetables, nuts, cereals, and bean. Both types of SNPs were evaluated for their impact on the NADPH-dependent glutathione reductase-mediated xenobiotic detoxification system (GSH-GSSG) in <i>A. niger</i> . At sub-inhibitory concentrations, both SNPs significantly inhibited fungal growth and spore formation. Additionally, they caused noticeable deformities on the surface of conidiophores ¹⁵ .
	Antimicrobial	Unpurified, purified sulphur and Gandhaga mezhugu was studied by agar diffusion method at various concentrations against <i>Escherichia Coli</i> , <i>P. Vulgaris</i> , <i>Klebsiellia Pneumoniae</i> , <i>Staphylococcus aureus</i> , <i>S.mutans</i> and <i>Candida albicans</i> the results showed significant antimicrobial activity ¹⁶ .
	Anti cancer	Apoptosis and growth inhibition effects of purified sulphur was observed on Human keratinocyte cells by MTT assay, Western blotting, Nuclear staining and cell cycle analysis ¹⁷ . In A375 malignant melanoma and MCF & breast cell line SNP inhibited the proliferation with copper arrest ¹⁷ .
	Anti tumour and antioxidant activity	5 mg/kg of SNP reduced the Ehrlich ascites in mice by increasing SOD, GPX and TAC production. It also increased P53 and Cytochrome C ¹⁷ .
TIN/Stannum	Antibacterial activity	SnO2 extracted and evaluated inactivation efficacy against <i>Escherichia coli</i> and <i>Staphylococcus aureus</i> under UV irradiation and dark and colony per unit was calculated. The results were found to be significant. SnO2 inhibited both bacteria ¹⁸
	Anticancer activity	SnO2 NP was extracted from <i>Annona squamosa</i> and studies for Cytotoxicity in HepG2 cell lines Via MTT assay and found the IC 50 value as 148µg/dl ¹⁹ .
	Anticancer activity	SnO2 NP - 3 samples was studies against HCT116 and A549 cell lines. The IC 50 values were 165, 1174, 208 µg/dl for HCT116 and 135, 157, 187 µg/dl for A549 respectively ¹⁹ .
	Antioxidant activity	SnO2 NP exhibited significant antioxidant activity through DPPH assay ¹⁹ .

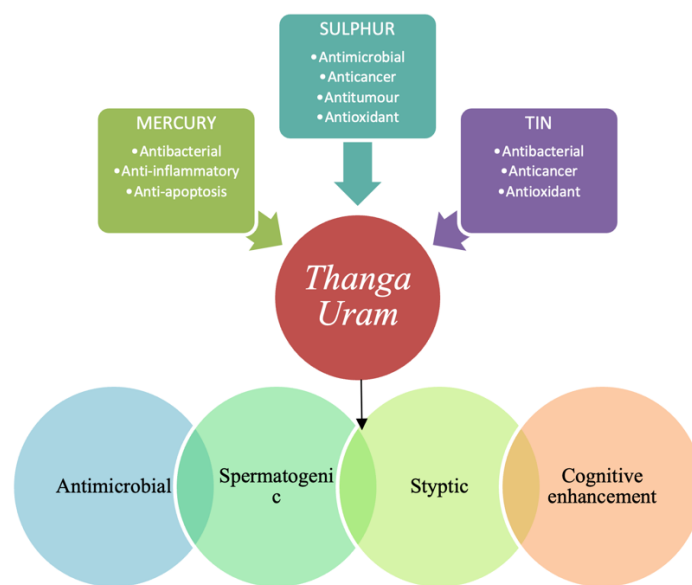


Figure 1: Pharmacological action of ingredients of thanga uram and thanga uram

Preparation: The procedure of TU preparation among the traditional healer Dr. C Shanmugam in Cuddalore was documented since at that time the market availability of the medicine was not available²⁰.

Characterization: The biochemical parameters of TU, revealed the existence of acid radicals such as phosphate, sulphide, and nitrite, as well as basic radicals such as iron²¹.

Similarly another study showed the presence of basic radicals like ammonium, magnesium, aluminium, calcium iron and zinc as well as acid radicals like phosphate and carbonate²².

The physicochemical analysis of TU showed that it is mosaic gold in colour without any odour. It was soluble in ghee and honey but insoluble in acetone and ether. The pH was found to be 4.65 thus,

having acidic nature it would be readily absorbed in stomach. Loss on drying was found to be 1.68% which shows the less moisture content thus curbs the microbial growth²¹.

The instrumental analysis was assessed to characterize TU. XRD and FTIR analysis of the drug was done. The results of FTIR research revealed the presence of a stretching O-H and C=H group. The X-ray diffraction study revealed that the medication was crystalline, and the elements lead, sulphur, and mercury was found at 2-Theta values of 29.59, 20.65, and 27.10^{21,23}.

PHARMACOLOGICAL ACTIVITY OF THANGA URAM

Anti-microbial activity

Due to the antimicrobial resistance along with the scarcity of newly developed antimicrobial drugs, there is a great threat for

both human and animals. Thus, there is a need of the hour to assess the anti-microbial agents effective in the treatment of diseases. Various Siddha formulations possess this antimicrobial resistance. One such proven Siddha metallo-mineral formulation is TU²⁰.

The anti-microbial activity was determined by employing the agar well diffusion method against the following microorganisms: *Escherichia coli*, *Klebsiella sps*, *Proteus vulgaris*, *Pseudomonas*, and *Staphylococcus aureus*, and fungal sps, *Candida albicans*. MIC values were discovered to be less than 8mm. In *Escherichia coli*, a higher MIC value was noted²⁰.

The antimicrobial activity of TU was investigated at different doses using the agar diffusion method. Bacteria including *Salmonella typhi*, *Escherichia coli*, and *Staphylococcus aureus* were chosen for this investigation, along with the *Candida albicans* fungus. By assessing the zone of inhibition concerning the standard medicines, the sensitivity was evaluated. However, bacteria and fungus showed less sensitivity than the conventional drugs streptomycin 10µg and Amphotericin 10µg, respectively²¹.

Also, from the review of ingredients of TU, Mercury is recognised for its wide ranging antimicrobial activity, sulphur possesses both antibacterial and antifungal activity and tin acts as a broad spectrum antibiotic (Table 2).

Spermatogenic activity

Among human infertility, 50% accounts for male infertility, among them 40-50% of cases, the aetiology of infertility remains undefined. Even though a broad range of strategies are carried out to overcome male infertility there is still a lack in success rate. Many formulations are indicated for the treatment of infertility in the Siddha system of medicine. One such Siddha Metallo-mineral formulation is TU²⁴.

24 Wistar albino rats were split into 4 groups to evaluate the spermatogenic activity of TU for 60 days: Control, Ethanol-induced, TU (23 mg/kg/day), and TU (46 mg/kg/day). The study discovered that Thanga uram acts by raising the quantity of spermatozoa in seminiferous tubules, as evidenced by an increase in spermatogenic components in comparison to the control group. There is a statistically significant approach to boost the amount and quality of sperm²⁴.

Cognitive enhancement activity

The demands on cognitive functions, which developed for a fundamentally different environment, are growing as the world gets more complex. There is a constant increase in the need for cognitive functioning in our increasingly complex information culture. Many methods to improve brain function have been put out in recent years. Siddha system of medicine long established the usage of herbs, metallic, and mineral formulations for enhancing memory function. However, only a few formulations are proven scientifically for their neuro-enhancement activity.

The memory enhancement activity of TU was studied using Hebb's William maze in Wistar albino rats. The rats were divided into 4 groups, with 6 rats in each (Control, Piracetam (Standard), TU (23 mg/kg/day), and TU (46 mg/kg /day)). The drug was administered for 7 days, and on the eighth day, the time taken to reach the reward chamber (TRC) in Hebb's William maze was calculated. Group 3 (TU 23 mg/kg) exhibits no discernible alterations in comparison to the control group. Meanwhile, at TU 46 mg/kg, the TRC was 25.83 ±12.20, considerably lower than the control group but higher than the standard (Piracetam - 19.16± 8.56). The investigation concluded that the medicine was effective at improving memory²⁵.

Styptic activity

Haemorrhage is one of the potential and leading causes of death throughout the world. Blood loss, while minor in everyday intraabdominal haemorrhage, piles, menorrhagia, cuts, and bruises, is one of the main causes of ill-health. Haemorrhage threatens the lives of patients and the injured in trauma care and surgical intervention. Haemorrhage is the primary cause of death in 48 hours after trauma, which accounts for 80% of all trauma accidents. Thus, styptic drugs will be helpful in the cessation of bleeding²¹.

The *in-vivo* styptic activity of TU was evaluated in 24 mice aged 9 to 12 months. Mice were grouped as 4: control, TU 500 mg/kg, TU 1000 mg/kg, and normal saline. The trial drugs were administered to the mice for three days, after which they were fasted for sixteen hours and dissected. Next, a liver ulcer was created, and its bleeding duration was observed. According to the findings of the study, the effectiveness of the trial drug in halting the bleeding appears to be greater at higher dosages²¹.

SAFETY STUDIES ON THANGA URAM

Toxicity study

Pre-clinical toxicity studies are crucial for determining a safe dose for human trials. Since the Siddha system of medicine opts for reverse pharmacology scientific evidence needs to be documented for the safety of patients and globalization of the System.

A comprehensive investigation of TU into the acute and sub-acute toxicity study based on OECD guidelines was done. Observations revealed slight differences in body weight between the treated groups and of TU in Wistar albino rats. In this study, rats were administered varying doses of Thanga uram (250, 500, and 1000 mg/kg) over a control group. Notably, rats receiving 1000 mg/kg exhibited a minor weight loss in the second week, although overall, all groups showed a steady increase in body weight, suggesting normal growth patterns likely supported by increased food and water intake. Furthermore, haematological analyses conducted as part of the toxicity assessment indicated no signs of toxicity. Histopathological examinations of tissue samples also did not reveal any significant pathological abnormalities, affirming the safety profile of TU at the doses tested²¹.

Also, the toxicity study was carried out based on WHO guidelines with Wistar albino rats of 6-8 weeks old and 160-180g weight. In acute toxicity, a single dose of (500mg/kg body weight) was administered then observed for 14 days and no abnormality was observed. Thus, the LD50 will be more than 500mg/kg²².

Long term toxicity for 90 days was carried out with 10 in each group (I - Control, II – TU 50mg, III - TU 250mg, IV – TU 500mg). After 90 days the animals were sacrificed and assessed for biochemical, physiological and histopathological changes. No abnormality or pathological or histopathological changes were found. Haematological assessment showed an increase in RBC level in group III. The biochemical analysis showed an increase in total cholesterol and LDL level¹⁹. These findings underscore the importance of pre-clinical toxicity studies in establishing the safety and dosage parameters of medicinal formulations like TU, crucial steps in advancing Siddha medicine globally through evidence-based practices²².

CLINICAL STUDY ON THANGA URAM

Clinical study

The effectiveness of TU was studied in conjunction with parangipattai leghiyam in treating 30 patients for Perumbaadu

rogam, or menorrhagia. The present study provides clinical validation for the efficacy of the experimental medicine in mitigating the major symptoms of menorrhagia, such as prolonged and heavy menstruation, lower abdominal discomfort, and low back pain. Following up with the OP, it was found that none of the patients' problems had relapsed. There were no known contraindications for the trial drug. Beneficial results from the study included elevated blood hemoglobin levels²¹.

DISCUSSION

Thanga Uram, a revered metallo-mineral formulation in Siddha medicine, stands out for its diverse and scientifically validated therapeutic properties. In Siddha medicine, the principles of Vali, Azhal, and Iyam humors are foundational for comprehensive health management. According to Siddha philosophy of taste, TU incorporates ingredients known for their bitter taste (kaippu), which are crucial for restoring balance and preventing the recurrence of diseases associated with imbalances in the vitiated azhal and iyam humors. TU is indicated for conditions like leucorrhoea, which is often attributed to elevated azhal²⁶. The bitter taste of TU helps in alleviating the vitiated azhal. According to the Panchabootha theory (5 elements – Fire, Air, Space, Earth, Water) and Panchabootha pancheekaranam, the genital organs are considered organs of "aagaya bootham(space)". Infertility may arise from a depletion of "aagaya bootham (space)" in the genital region. The bitter taste composed of "kaatru (air)" and "aagaya bootham (space)", suggests that it may help regulate the depleted "aagayam (space)", thereby potentially treating infertility²⁷. As it is biotransformed to Kaarpu taste it may enhance the appetite as indicated. The major ingredient mercury is traditionally administered in the treatment of syphilis thus; TU may also be administered for syphilis (Megam)⁹.

Previous research on the whole formulation and each ingredient has substantiated its efficacy across several fronts: it exhibits potent antimicrobial activity, which enable it to combat a wide range of microbial infections effectively. Additionally, supports reproductive health by enhancing spermatogenesis, acts as a styptic agent that promotes tissue contraction to manage wounds and conditions like menorrhagia effectively. Its cognitive enhancement properties suggest it can improve cognitive functions such as memory and focus. Biochemical analysis has identified key components within TU including phosphate, sulphide, nitrite, and iron. These elements play crucial roles in various physiological processes, potentially contributing to its therapeutic effects. Safety assessments through toxicity studies have consistently demonstrated safety profile for TU reassuring its suitability for therapeutic use. Also, this study showed elevated levels of RBC in mid dose group and the presence of iron may help in treating anaemic conditions. In clinical practice, TU is prescribed for conditions such as leucorrhoea and urogenital diseases, where it's antimicrobial and styptic properties are particularly beneficial. Moreover, as a tonic, TU supports overall health and vitality, while its role as a brain enhancer suggests benefits for cognitive health²¹⁻²⁵.

Overall, TU emerges as a versatile Siddha remedy with a robust scientific basis, offering a holistic approach to health promotion and disease management across multiple domains. Its diverse properties and safety profile underscore its potential as a valuable addition to therapeutic strategies aimed at enhancing well-being.

CONCLUSION

The examination of Thanga Uram, underscores its profound therapeutic potential across a spectrum of ailments. Supported by rigorous scientific inquiry, including antimicrobial assays,

spermatogenic activity, memory enhancement investigations, and toxicity evaluations, TU emerges as a versatile remedy with promising efficacy and safety profiles. Furthermore, clinical trials validate its effectiveness in addressing conditions such as menorrhagia, further cementing its relevance in modern healthcare. With its deep-rooted tradition complemented by contemporary scientific validation, TU stands as a valuable asset in the realm of Siddha medicine, offering comprehensive solutions for diverse health challenges.

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