INFORMATICS JOURNALS

Short Review

Journal of Natural Remedies
DOI: 10.18311/jnr/2026/55774

eISSN: 2320-3358 | Vol 26(8), 2026 | pp. 2041-2051

Pearl as a Therapeutic Biomineral: A Review of its Pharmacological Potential

Sasikumar Palanivel[1*], Amala Hazel Amaladason Mary Alphonsal[2], Mahalakshmi Varadhan[3], Manikgantan Erulandy Muthiah[4] and Amudha Palanivelu[5]

[1]Department of Kuzhanthai Maruthuvam (Siddha Paediatric), National Institute of Siddha, (Affiliated with The Tamil Nadu Dr. M. G. R Medical University), Ministry of Ayush, Chennai - 600047, Tamil Nadu, India; sasikumarvel1994@gmail.com

[2]Department of Sool and Magalir Maruthuvam (Siddha Obstetrics and Gynaecology), National Institute of Siddha, (Affiliated with The Tamil Nadu Dr. M. G. R Medical University), Ministry of Ayush, Chennai - 600047, Tamil Nadu, India

[3]Department of Siddhar Yoga Maruthuvam, National Institute of Siddha, (Affiliated with The Tamil Nadu Dr. M. G. R Medical University), Ministry of Ayush, Chennai - 600047, Tamil Nadu, India

[4]Department of Siddha, The Tamil Nadu Dr. M. G. R Medicine University, Guindy, Chennai - 600032, Tamil Nadu, India

[5]Department of Pharmacology, C. L. Baid Metha College of Pharmacy (Affiliated with The Tamil Nadu Dr. M. G. R. Medical University), Chennai - 600097, Tamil Nadu, India

Abstract

Background: Pearl, known as *Muthu* in *Siddha* medicine and *Mukta* in *Ayurveda*, is a biogenic calcium-based biomineral traditionally used for the management of neurological, ocular, inflammatory, and degenerative disorders. Classical medical systems attribute cooling, rejuvenating, and life-supportive properties to pearl-based formulations. Recent scientific investigations have explored the pharmacological potential of pearl and its processed preparations. **Aim:** To critically review and integrate traditional *Siddha* knowledge with contemporary physicochemical, pharmacological, and toxicological evidence regarding the therapeutic potential of pearl-based formulations. **Methods:** A comprehensive literature review was conducted using classical *Siddha* texts and published scientific studies addressing pearl composition, purification and preparation methods, physicochemical characterisation, pharmacological activities, and toxicological safety. **Results:** Available evidence indicates that pearl-based formulations possess antioxidant, anti-inflammatory, immunomodulatory, neuroprotective, hepatoprotective, osteogenic, wound-healing, anti-cataract, and anticancer activities. Modern analytical studies demonstrate that properly processed pearl formulations are predominantly calcium-rich, biocompatible, and free from toxic heavy metals. Experimental findings support several traditional therapeutic claims, although most evidence is derived from *in vitro* and animal studies. **Conclusion:** Pearl-based formulations represent promising therapeutic biominerals with substantial traditional and emerging scientific support. However, further standardisation of preparation methods, mechanistic investigations, and well-designed clinical studies are necessary to establish their efficacy and facilitate evidence-based integration into contemporary healthcare.

Major Findings: Pearl-based formulations, particularly *Muthu Parpam*, show promising antioxidant, anti-inflammatory, neuroprotective, hepatoprotective, osteogenic, wound-healing, anti-cataract, and anticancer activities. However, evidence is largely preclinical, requiring standardised preparation and well-designed clinical studies.

Keywords: Biomineral, Calcium Carbonate, Integrative Healthcare, *Parpam* Preparation, Pearl, *Muthu*, Pharmacological Activities, Toxicological Safety, Traditional Medicine

(Article Chronicle: Article Received on: 09.04.2026; Revised on: 11.06.2026; Accepted on: 20.06.2026)

**Author for correspondence*

1. Introduction

Pearl, a biogenic calcium carbonate mineral known as *Mukta* in *Ayurveda* and *Muthu* in *Siddha* medicine, has been revered for centuries across multiple traditional medical systems, including *Siddha*, *Ayurveda*, *Unani*, and Traditional Chinese Medicine, for its cooling, rejuvenating, and life-sustaining properties. Classical texts describe pearl-based formulations as agents that calm the mind, strengthen the body, enhance vitality, support ocular and cardiac health, and restore humoral balance, particularly in heat- and stress-related disorders. Beyond traditional usage, pearls have also attracted considerable interest in modern biomedical research due to their excellent biocompatibility, unique organic-inorganic composition, and biomineralised nacre architecture, which emphasises their applications in tissue engineering, wound healing, bone regeneration, dermatology, and immunomodulation[1,2]. Despite the growing body of experimental evidence demonstrating the antioxidant, anti-inflammatory, immunomodulatory, neuroprotective, hepatoprotective, osteogenic, and regenerative properties of pearl-based formulations, the available literature remains highly fragmented[3-6]. Most studies are discipline-specific, focusing either on traditional descriptions without mechanistic validation or on isolated pharmacological outcomes without adequate linkage to classical preparation methods and therapeutic doctrines. Furthermore, variations in purification, calcination, particle size, and analytical characterisation contribute to inconsistencies in reported efficacy and safety profiles, limiting translational relevance.

This review is therefore important to systematically integrate traditional *Siddha* knowledge with contemporary physicochemical, pharmacological, and toxicological evidence, offering a unified and critical appraisal of pearl as a therapeutic biomineral. By identifying convergences across traditional medical systems and modern scientific findings, and by highlighting existing research gaps, particularly the scarcity of standardised preparation protocols, mechanistic studies, and well-designed clinical trials, this review aims to provide a robust evidence base to guide future research and facilitate the rational integration of pearl-based medicines into evidence-informed healthcare.

1.1 Mechanism of Pearl Production

Pearls are unique organic-inorganic biominerals formed through highly regulated biomineralisation processes. This process involves the coordinated activity of epithelial cells, proteins, and mineral deposition systems that enable organisms to produce mineralised tissues such as nacre. In the case of pearls, biomineralisation is initiated when the mantle tissue of a shellfish undergoes injury or is exposed to a foreign stimulus. This triggers a defensive response in which the epithelial cells of the mantle fold inward to form a pearl sac, which subsequently secretes successive layers of nacre around the irritant[7]. The formation of pearls in natural environments is rare, making artificially induced pearl culture the predominant method of production. When an external body, either naturally occurring debris or an implanted nucleus, enters the shell, the upper mantle tissue envelopes it, forming the initial pearl sac. This sac continually secretes calcium carbonate and organic matrix substances that gradually build the pearl structure. Pearl formation proceeds in two major stages: an initial irregular deposition of calcium carbonate on the bare nucleus, followed by a more ordered and rhythmic laying down of aragonite tablets that ultimately produce mature nacre, similar to shell regeneration[7-9]. The entire process typically requires 2-3 years and is regulated by a network of genes and matrix proteins that influence nacre secretion, crystal orientation, growth rate, and overall pearl morphology. Several genes, including Hic14, Hic19, and Pif80, and matrix proteins such as pearlin and shell matrix proteins have been identified as primary regulators that govern crystal nucleation and layering, thereby determining the quality and characteristics of pearl[2].

1.2 Structural Characteristics of Pearl

Structurally, pearls consist of three major components: the nucleus, the amorphous matrix layer, and the nacre layer. The nucleus, which may be naturally formed or intentionally implanted, provides the central core around which mineralisation occurs. Surrounding this is the amorphous matrix layer, composed of organic materials and microcrystalline deposits; its thickness influences pearl quality, being notably thinner or absent in high-grade pearls. The nacre layer, which forms the

main bulk of the pearl, comprises both prismatic and aragonite layers. While the prismatic layer contributes to structural orientation, the aragonite layer is responsible for the lustre and optical qualities of the pearl is the most critical determinant of quality[8].

1.3 Characteristics of Pearls

Pearl is characterised by its colour, lustre, shape, hardness, texture, toughness, and specific gravity[10,11].

Lusture: According to Rasa Paddhati, *Mukta* has three types of lusture, *viz*, *Madhuchaayae*. just like honey, *Sitachaaya*, *i.e.*, just like sugar and *Shrikhandachaaya*, *i.e.*, just like a preparation made up of sugar and curd.

Colour: Colour for freshwater can be peach, black, lavender, white or pink.

Shape: Round is the most favoured and valuable. Baroque or irregular or potato shapes are some of the names given to odd-shaped pearls. Oval shaped pearls are sort of like an egg. Button-shaped are round but a little flat. Some are round on the top and flat on one side. Tear-drop shapes lend themselves.

Hardness: 2.5-4

Texture: Slightly rough

Toughness: Fair, soft and easily damaged by acid and skin oil.

Specific Gravity: Varies with source and with the type of nucleus; the naturally occurring range from 2.66-2.78, whereas cultured pearls range from 2.72-2.78.

1.4 Organic Constituents of Pearls and Their Biological Significance

Pearls contain a relatively small proportion of organic matter (generally less than 5%), which consists primarily of proteins, polypeptides, amino acids, vitamins, porphyrins, and metalloporphyrin compounds. Although present in minor quantities, these organic constituents play an important role in the biological and pharmacological activities attributed to pearls.

Hydrolysis of pearl proteins releases several essential amino acids, including lysine, phenylalanine, methionine, threonine, isoleucine, leucine, and valine, along with non-essential amino acids such as aspartate, serine, glutamate, proline, glycine, cysteine, alanine, tyrosine, histidine, and arginine. Freshwater pearls have also been reported to contain taurine, a biologically active non-protein amino acid. These amino acids contribute to cellular metabolism, tissue maintenance, antioxidant defence, and physiological homeostasis.

Pearl-derived proteins and polypeptides have attracted considerable attention due to their potential health-promoting properties. Experimental studies suggest that these bioactive molecules may contribute to tissue regeneration, wound healing, immunomodulation, and cellular protection. In addition, the vitamin B complex supports various metabolic processes, while porphyrin and metalloporphyrin compounds possess antioxidant and immunomodulatory properties. Although the organic matrix constitutes only a minor fraction of the pearl, it is believed to play a crucial role in many of its biological activities and may act synergistically with the mineral components to produce the diverse therapeutic effects reported for pearl-based formulations[11-13].

1.5 Traditional Purification Methods of *Muthu*

i. Soak the *Muthu* separately in lemon juice and vinegar (*Kaadi*), each for one day. Then wash it with water[14].
ii. Pour 105 g of fermented curd to 35 g of *Muthu*. Insolate it for 3 days, with fresh curd being added on each day. Then dry it in sunlight without adding curd for the next two days. The same process is repeated two more times. Dry it and rinse it off well[15].
iii. Soak the *Muthu* in *Sangam* fruit juice (*Azima tetracantha*) or Ponampazha juice (*Neikottan*) (*Sapindus trifoliatus*) or *Puli Kuzhampu* for 2 days to get the purified gem[15].
iv. Soak the *Muthu* in unripe fruit juice of *Oomathai* (*Datura metel*) for one day. On the next day, wash it in pure water. Soak it again in tamarind leaf juice for one day. Then rinse it off with pure water and dry it under sunlight[15].
v. Soak the *Muthu* in *Sangam* fruit juice (*Azima tetracantha*) or tamarind fruit juice for 3 days to get the purified gem[16].
vi. Soak the *Muthu* in *Sangam* fruit juice (*Azima tetracantha*), *Poovandhi* fruit juice (*Sapindus trifoliatus*) and Tender coconut water separately for 3 days to get the purified gem[17].
vii. Soak the *Muthu* for 2 days in *Neikottan* fruit juice (*Sapindus trifoliatus*) or *puliaarai* juice (*Oxalis corniculata*) to get the purified gem[17] (Figure 1).

1.6 Various Preparations of *Muthu Parpam*

Preparation - 1

Take one *balam* (35 g) of *Muthu* powder and two quantities (70 g) of *Nochiyilai* (*Vitex negundo*), extract their juice, and let it soak for two days. Then, grind with *nochi* leaf juice for two days. Then, it is made into small cakes and dried for 2 days, and subjected to incineration with 40 cow dung cakes. After that, grind the obtained powder with *Curculigo orchioides* (*Nilappanai* tuber) juice as mentioned above and subject to incineration as above[15].

Preparation - 2

Purified pearl is ground with *Sinaplis alba* for3 days and made into small cakes and subjected to incineration[15].

Preparation - 3

Purified pearl is ground with milk for 3 days and made into small cakes and subjected to incineration[15].

Preparation - 4

Purified pearl is ground with rose water for 8 days and dried as powder[15].

Preparation - 5

Take one *balam* of *Muthu* and grind with *Trianthema decandra* plant juice for 5 days, made into small cakes and dried, then subjected to incineration with 9 *varattis*. Then again grind with *Calotropis gigantea* plant juice like above and subjected to incineration with 8 *varattis*. Similarly, with *Ficus religiosa* leaf juice and *Terminalia arjuna* bark juice and incinerated with 7 and 6 varattis respectively[15].

1.7 Pearl in *Siddha* Medicine

In *Siddha* medicine, *Muthu* (pearl) is classified under the *Thathu* (metal/mineral) and *Uyir Porul* (marine-derived) categories, possessing cold potency and profound life-supporting qualities. *Siddha* literature

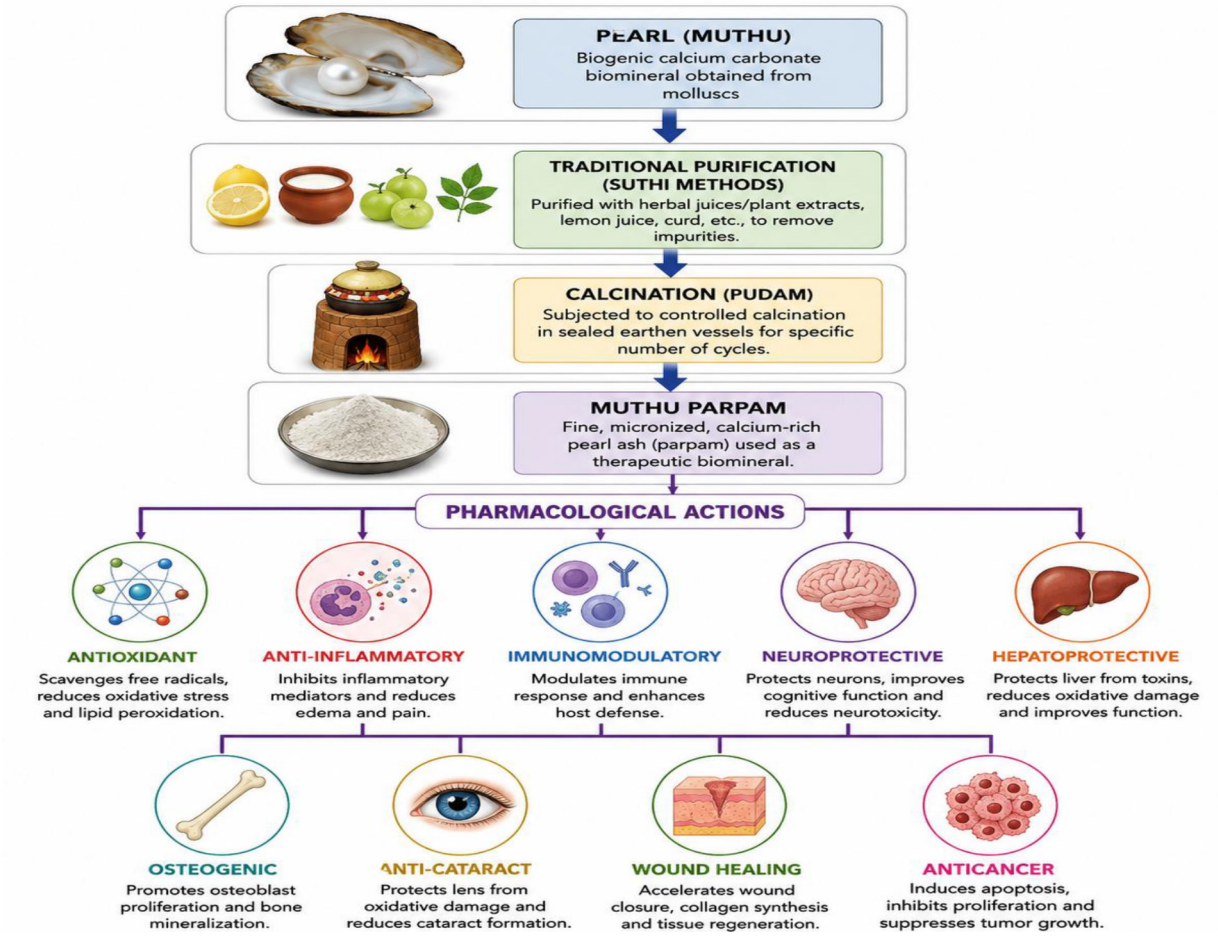


Figure 1. Schematic representation of pearl processing and pharmacological activities of *Muthu Parpam*.

such as *Agathiyar Gunavagadam, Theriyar Yamaga Venba, Siddha Materia Medica, and Kannusamy Parambarai Vaidhiyam* describes *Muthu* as a superior drug that enhances physical strength, stabilises mental functions, improves complexion, and restores deranged humours, especially *Pittam* and *Azhal*. In *Siddha* literature, *Muthu* (pearl) is ascribed an exceptional therapeutic stature. Classical texts often juxtapose its potency with that of mercury, emphasising that pearl embodies a unique lunar energy. This association with the moon symbolises its cooling, stabilising, and rejuvenating influences, underscoring its supremacy among mineral-based medicines within the *Siddha* system.

1.8 Physicochemical Characterisation and Elemental Composition

Pearl-based *Siddha* formulations have been extensively characterised using modern analytical techniques to establish their chemical composition, elemental profile, and safety. Studies have demonstrated that pearls consist predominantly of calcium carbonate (approximately 95%), primarily in the aragonite crystalline form, with smaller quantities of magnesium carbonate and other inorganic constituents. Trace elements such as sodium, manganese, selenium, copper, iron, and phosphorus are also present. Analytical investigations using ICP-OES have further confirmed the absence of toxic heavy metals such as arsenic, mercury, lead, and cadmium in properly prepared *Muthu Parpam*, supporting its safety for therapeutic use[18].

Parallel characterisation studies on pearl powder indicate that pearls consist of approximately 95% calcium carbonate, primarily in the aragonite polymorphic form, with magnesium carbonate as a secondary mineral component. Additional inorganic constituents include calcium phosphate, silica, aluminium oxide, and iron oxide, along with trace elements such as sodium, manganese, selenium, aluminium, and copper. The remaining fraction is an organic matrix composed of proteins, glycoproteins, polysaccharides, peptides, and amino acids, which significantly influence biological activity[12].

Biochemical analyses have identified essential and hydrophobic amino acids such as aspartate, glutamate, cysteine, methionine, tryptophan, phenylalanine, leucine, isoleucine, and valine. Aspartate and glutamate exhibit antioxidant properties, while hydrophobic amino acids contribute to free-radical quenching. A key protein component, conchiolin, composed of 17 amino acids, has been proposed as a major contributor to wound healing and collagen regeneration[1].

Structurally, pearl powder exists in different calcium carbonate polymorphs—aragonite, vaterite, and calcite. Aragonite is predominant in high-quality pearls and contributes to biological activity, whereas vaterite is unstable in aqueous environments and calcite is thermodynamically stable but biologically less active. The nacre layer of pearls represents a block-and-mortar bio composite architecture with superior osteogenic potential compared to hydroxyapatite[1].

2. Pharmacological Activity

2.1 Antioxidant Activity

Antioxidant activity is one of the most consistently reported pharmacological properties of pearl-based formulations. Chitra *et al.*[19] evaluated the *in vitro* antioxidant activity of *Muthu Parpam*, a calcined preparation derived from *Pinctada* species, using standard free-radical scavenging assays. The formulation exhibited significant antioxidant potential in a concentration-dependent manner. The authors attributed this activity to calcium carbonate, trace minerals, and organic matrix components capable of neutralising reactive oxygen species and preventing oxidative damage[19]. Additionally, another study on pearl powder restored antioxidant defences by preserving superoxide dismutase activity and glutathione levels suppressed by AAPH[20]. The same study also demonstrated that *Mukta Bhasma* possesses strong antioxidant activity in CCl_4-induced oxidative stress. Treatment with MB (*Mukta Bhasma*) at 200 mg/kg significantly decreased lipid peroxidation levels while concomitantly enhancing endogenous antioxidant defences, as evidenced by increased reduced glutathione and catalase activities ($p<0.001$). These biochemical changes indicate effective attenuation of oxidative damage and restoration of redox balance in hepatic tissue, suggesting that the antioxidant potential of *Mukta Bhasma* contributes substantially to its overall hepatoprotective efficacy[5].

2.2 Anti-hemolytic Activity

Pearl powder has been evaluated for its *in vitro* anti-haemolytic and antioxidant effects using human erythrocytes exposed to AAPH-induced oxidative stress. Pretreatment with pearl powder (50-200 µg/ml) significantly and dose-dependently inhibited AAPH-induced hemolysis. Pearl powder markedly reduced lipid peroxidation, evidenced by decreased malondialdehyde levels, with 200 µg/ml showing values comparable to control. It also protected erythrocyte membrane proteins by preventing high-molecular-weight protein aggregation and restoring normal protein profiles[20].

2.3 Anti-inflammatory and Anti-fibrotic Activity

The anti-inflammatory potential of pearl-based *Siddha* formulations has been validated through experimental animal models. *Muthu Parpam* was evaluated using the carrageenan-induced hind paw oedema model in Wistar rats at doses of 100, 200, and 400 mg/kg**,** with indomethacin (10 mg/kg) as the standard drug. The formulation produced a dose- and time-dependent inhibition of paw oedema, with maximum activity observed at 5 h post-carrageenan injection. Percentage inhibition values were 13.95%, 25.12%, and 46.05% for the respective doses, compared to 52.30% inhibition by indomethacin. These findings suggest inhibition of prostaglandin synthesis and cyclooxygenase pathways, indicating NSAID-like anti-inflammatory action[21].

In addition to inflammation control, pearl powder has demonstrated anti-fibrotic activity**,** characterised by reduced excessive collagen type I deposition and enhanced matrix metalloproteinase activity. Magnesium content and anti-apoptotic effects further contribute to modulation of inflammatory and fibrotic pathways during tissue repair[22].

2.4 Immunomodulatory Activity

A study on the *Ayurvedic* formulation *Mukta Bhasma* (calx of cultured pearl) was conducted to evaluate its *in vitro* immunomodulatory activity on human neutrophils, highlighting its relevance in immune activation against emerging infectious diseases. *Mukta Bhasma* was tested at five different doses (1, 0.5, 0.25, 0.125, and 0.06 mg) using standard immunological assays, including the Nitroblue Tetrazolium (NBT) test, phagocytosis and candidacidal assays, and neutrophil locomotion and chemotaxis assays. The findings revealed a highly significant enhancement ($p<0.001$) in NBT-stimulated cells, phagocytic activity, candidacidal action, and neutrophil chemotaxis, particularly at the lowest dose of 0.06 mg. Lower doses consistently showed superior immunostimulatory effects compared to higher doses[5].

A study demonstrated that Hydrolysed Seawater Pearl Tablets (HSPT) exert significant immunomodulatory effects in a cigarette smoke-induced Chronic Obstructive Pulmonary Disease (COPD) mouse model. HSPT treatment markedly attenuated airway inflammation, as evidenced by reduced inflammatory cell infiltration in lung tissue and a significant decrease in eosinophils, lymphocytes, neutrophils, and macrophages in bronchoalveolar lavage fluid. In parallel, HSPT suppressed both Th1- and Th2-associated cytokines, lowering the levels of IFN-γ and IL-2 as well as IL-4 and IL-10 in serum and lung tissues, with corresponding reductions in cytokine expression in the spleen and lung. Moreover, HSPT decreased the proportion of $CD3^+CD4^+$ T cells and effectively restored the Th1/Th2 immune balance disrupted by cigarette smoke exposure[22].

Similarly, another study showed that Pearls in Ashed Form (PAF) act as a safe and effective oral immunomodulator. Oral administration enhanced innate and adaptive immune responses by upregulating TLR-2, increasing CD80/CD86 co-stimulatory signals, promoting T- and B-cell activation, and elevating both Th1 and Th2 cytokines, without significantly increasing inflammatory cytokines or inducing toxicity. These findings indicate that PAF functions as a balanced Th1/Th2 immune regulator with potential clinical relevance [19]. Additionally, a study showed that choline modulates immune responses in pearl oysters by suppressing pro-inflammatory cytokines (TNF-α, IL-17), inhibiting key immune signalling pathways, and enhancing antioxidant enzyme activity, while regulating intracellular calcium levels and improving nucleus retention after transplantation, indicating its protective immunoregulatory role[23].

2.5 Hepatoprotective Activity

A study demonstrated that an *Ayurvedic* formulation, *Mukta Bhasma* (MB), exhibits significant

hepatoprotective activity against carbon tetrachloride (CCl_4)-induced hepatic injury in Wistar albino rats. Oral administration of MB for 10 days, particularly at a dose of 200 mg/kg, markedly restored serum biochemical markers of liver function altered by CCl_4 intoxication. Elevated levels of SGOT, SGPT, alkaline phosphatase, total and direct bilirubin, total cholesterol, and triglycerides were significantly reduced ($p<0.001$) toward near-normal values, comparable to the standard hepatoprotective drug silymarin. Histopathological examination further supported these findings by showing a pronounced reduction in fatty degeneration and structural damage of hepatic tissue, confirming the protective effect of MB on liver architecture[5].

2.6 Wound Healing and Tissue Regeneration

Pearl powder, particularly in nanoscale form, exhibits pronounced wound-healing and regenerative properties. Nanosized pearl powder significantly enhances fibroblast proliferation and keratinocyte migration *in vitro* due to increased release of bioactive proteins from the organic matrix. In animal excision wound models, nano-pearl powder accelerated wound closure, improved collagen deposition, and enhanced angiogenesis, resulting in stronger regenerated tissue[12].

Histological analyses confirmed well-organised collagen architecture and increased neovascularisation in nano-pearl-treated groups. These effects are attributed to increased surface area, improved cellular uptake, enhanced protein solubility, and better tissue adherence compared to micro-sized pearl powder formulations[24].

2.7 Bone Health and Osteogenic Activity

Pearls have long been employed in traditional medical systems for the management of bone injuries and are increasingly recognised as effective osteogenic agents and bone grafting materials. Experimental studies have demonstrated that pearls possess superior bone-forming potential compared with conventional biomaterials. *In vitro* evaluations using simulated body fluid immersion and osteoblast cell cultures showed that pearls stimulate osteoblast proliferation more rapidly and consistently than shell nacre or hyaluronic acid. Clinically, pearls are commonly administered in powdered form, as the disrupted crystalline structure of pearl powder enhances osteoinductive capacity, while its chemical constituents—particularly in nano-sized formulations—are more readily bioavailable. Evidence from *in vivo* rabbit femoral defect models indicates that nano-pearl powder outperforms micron-sized pearl powder in new bone formation, degradation rate, and overall repair efficiency, highlighting its enhanced regenerative potential[6].

Nacre, the primary structural component of pearls, exhibits comparable osteogenic properties. Studies assessing bone-related gene expression have shown that nacre promotes the expression of key osteogenic markers, including alkaline phosphatase, bone sialoprotein, and osteocalcin, an effect attributed in part to its excellent biocompatibility and reduced particle size. Moreover, water-soluble organic matrices derived from pearls or nacre have been shown to induce differentiation and maturation of fibroblasts, bone marrow stromal cells, and osteoblasts, while also prolonging osteocyte survival. Mechanistic investigations suggest that these osteogenic effects are mediated through the promotion of MC3T3-E1 cell differentiation via autophagy, regulated predominantly through the MEK/ERK signalling pathway, underscoring the central role of these cells in bone formation[6,12].

In the context of bone grafting, pearl and nacre powders are frequently incorporated into composite scaffolds to enhance mechanical strength and biological performance. Composite materials such as polylactic acid-pearl or nacre scaffolds demonstrate significantly improved compressive strength and osteogenic activity compared with polymer scaffolds alone, alongside increased alkaline phosphatase activity and proliferation of mesenchymal stem cells. Similar osteo-enhancing effects have been reported for nano-nacre/type I collagen, nano-pearl/chitosan-hyaluronic acid, and growth factor-enriched pearl-based composites, all of which exhibit superior bone defect repair in animal models[6,12,13,25].

2.8 Neuroprotective, Cognitive, and Sedative Effects

Neuroprotective and sedative properties of pearl-based formulations are well documented across experimental models. Girija *et al.*[3] demonstrated that *Muthu Parpam* exhibits significant acetylcholinesterase inhibitory activity using the Ellman colorimetric method. The formulation achieved 71.68% inhibition at 500 µg/ml,

compared to 84.87% inhibition by physostigmine at 40 µg/ml, indicating notable neuroprotective potential and relevance in Alzheimer's disease management[2].

A study demonstrated, in parallel, that Morris water maze performance was significantly improved in insomnia-induced, sleep-deprived rats treated with Pearl Powder (PP) and Estazolam (ES) compared with sleep-deprived controls, indicating attenuation of cognitive deficits by both interventions. However, proteomic analysis revealed distinct pharmacological profiles, with pearl powder showing a greater capacity to normalise sleep-deprivation-induced aberrant gene expression than estazolam. In parallel, protein-protein interaction and pathway enrichment analyses indicated that pearl powder more effectively rescued multiple pathways disrupted by sleep deprivation, including retrograde endocannabinoid signalling and interaction networks associated with oxidative phosphorylation and neurodegenerative disease-related pathways such as Parkinson's and Huntington's diseases[26].

2.9 Anti-cataract Activity

Anti-cataract activity of pearl-based formulations has been demonstrated using isolated goat lens models. Chitra *et al.*[19] evaluated *Muthu Parpam* at concentrations of 100 µg/ml and 200 µg/ml under high-glucose-induced cataract conditions. The formulation reduced lens opacification in a dose-dependent manner and exhibited aldose reductase inhibitory activity with an IC_{50} of approximately 558 µg/ml, indicating modulation of the polyol pathway involved in cataractogenesis. These findings validate traditional applications in eye disorders while highlighting the need for further *in vivo* and clinical studies[26,27].

2.10 Anticancer Activity

Muthu Chenduram was evaluated for *in vitro* anticancer activity against cervical cancer using HeLa cell lines. The formulation produced dose-dependent cytotoxicity, with a significant reduction in cell viability and an LC_{50} value of approximately 66.77 µg/ml. Treated cells exhibited apoptotic morphological changes, including nuclear condensation and cell shrinkage. Flow cytometric analysis revealed a substantial increase in late apoptotic cell populations compared to untreated controls, confirming apoptosis-mediated cytotoxicity[28].

2.11 Toxicological Evaluation

Comprehensive safety evaluations indicate that pearl-based formulations possess a wide safety margin. Acute and subacute toxicity studies of *Muthu Parpam* revealed no mortality or adverse behavioural changes. Nano-pearl powder demonstrated favourable biocompatibility in cytotoxicity assays, maintaining normal cell morphology without large-area detachment or structural damage; mild cytotoxicity was observed only at excessively high concentrations (500 µg/ml or undiluted extracts)[29].

Intradermal stimulation studies showed good local tolerance, with transient skin elevations resolving within 4 h and no erythema or oedema observed at 24, 48, or 72 h. Genotoxicity assessments confirmed the absence of mutagenic effects in mouse sperm, supporting the non-genotoxic nature of pearl-based preparations when properly processed[1].

3. Discussion

Muthu Parpam is a classical *Siddha* mineral formulation prepared from pearl through meticulously described purification and incineration (*pudam*) procedures. These traditional processes are not merely ritualistic but are designed to transform the raw biogenic calcium carbonate into a biologically compatible, fine, and therapeutically effective form. Modern analytical studies substantiate this transformation by demonstrating the predominance of calcium with the absence of toxic heavy metals, thereby validating the safety and scientific relevance of the classical preparation methods.

Traditional *Siddha* literature attributes cooling, rejuvenating, vision-enhancing, and mind-stabilising properties to *Muthu*. Modern pharmacological investigations provide partial scientific support for these claims. The documented antioxidant, anti-inflammatory, neuroprotective, anti-cataract, and osteogenic activities correlate with traditional indications for neurological disorders, ocular diseases, tissue degeneration, and inflammatory conditions. Such convergence between classical knowledge and contemporary biomedical evidence strengthens the therapeutic relevance of pearl-based formulations.

Pharmacological studies indicate that *Muthu Parpam* exhibits antioxidant, anti-inflammatory, neuroprotective, anti-cataract, and supportive

tissue-regenerative activities. These effects are generally moderate rather than aggressively pharmacodynamic, suggesting a regulatory and restorative mode of action. Such a profile aligns well with *Siddha* therapeutic philosophy, which emphasises long-term balance, humoral equilibrium, and rejuvenation rather than acute symptom suppression. From a *Siddha* concept, pearl is attributed to the lunar principle and described as possessing profound cooling, stabilising, and life-sustaining qualities. Classical texts elevate pearl by comparing its potency to mercury and symbolically associating it with sakthi (Parvathi), the nurturing, sustaining, and harmonising cosmic force. The cooling property ascribed to pearl may be correlated with its documented ability to reduce inflammatory mediators, oxidative stress, neuronal excitability, and excessive cellular proliferation. These actions are particularly relevant to *Pittam*- and *Azhal*-dominant disorders, which are characterised in *Siddha* medicine by heat, hyperactivity, and degeneration. Safety evaluations further reinforce the appropriateness of *Muthu Parpam* for long-term use, a critical consideration for mineral-based *Siddha* medicines. Acute and subacute toxicity studies report no mortality or significant adverse effects at therapeutic doses, supporting its traditional application in prolonged treatment regimens under medical supervision. Similar safety profiles reported in *Ayurveda* (*Mukta Bhasma*) and Traditional Chinese Medicine further strengthen the trans-cultural credibility of pearl-based therapeutics. The convergence of indications across *Siddha*, *Ayurveda*, and Traditional Chinese Medicine -particularly for mental disturbances, ocular disorders, debility, insomnia, and tissue weakness-suggests a shared empirical recognition of pearl's therapeutic value. This cross-system consistency enhances confidence in the biological relevance of pearl-derived medicines.

Recent advances in biomaterial and regenerative medicine research have expanded the therapeutic applications of pearl-derived materials. Pearl powder-incorporated scaffolds have been shown to promote osteoblast proliferation, osteogenic differentiation, angiogenesis, and immunomodulation while exhibiting excellent biocompatibility and safety profiles. These findings provide modern scientific support for the traditional use of pearl-based formulations in bone healing and tissue regeneration and highlight their potential role in future regenerative medicine applications[30,31].

However, despite extensive *in vitro* and animal-based evidence, human clinical studies remain limited. Variability in preparation methods, calcination parameters, and particle size may significantly influence efficacy and safety. Therefore, future research should prioritise standardised preparation protocols, advanced physicochemical characterisation, and well-designed clinical trials to translate traditional knowledge into evidence-based integrative therapeutics.

4. Conclusion

Muthu Parpam represents a scientifically promising *Siddha* biomineral formulation derived from pearl. Available experimental evidence supports its antioxidant, anti-inflammatory, immunomodulatory, neuroprotective, hepatoprotective, osteogenic, anti-cataract, wound-healing, and anticancer activities. Modern analytical studies further demonstrate its safety, biocompatibility, and calcium-rich composition following classical purification and calcination procedures. Although preclinical findings are encouraging, robust clinical trials and standardised manufacturing protocols remain necessary to establish therapeutic efficacy and reproducibility. Future research integrating traditional *Siddha* knowledge with advanced biomedical methodologies may facilitate the wider acceptance of pearl-based formulations in evidence-based integrative healthcare.

5. Acknowledgement

The authors acknowledge the support and facilities provided by the National Institute of *Siddha* (Affiliated with The Tamil Nadu Dr.M.G. R Medical University), Tambaram Sanatorium, Chennai, for their support in this study.

6. References

1. Loh XJ, Young DJ, Guo H, Tang L, Wu Y, Zhang G, Tang C, Ruan H. Pearl powder - An emerging material for biomedical applications: A review. Materials (Basel). 2021; 14(11):2797. https://doi.org/10.3390/ma14112797 PMid:34074019 PMCid:PMC8197316

2. Song Y, Chen W, Fu K, Wang Z. The application of pearls in traditional medicine of China and their chemical constituents, pharmacology, toxicology, and clinical research. Front Pharmacol. 2022; 13. https://doi.org/10.3389/fphar.2022.893229 PMid:36081944 PMCid:PMC9445187
3. Girija NS, Shanmugapriya P. Neuroprotective activity of *Siddha* herbo-mineral formulation *Muthu Parpam* through acetylcholine esterase enzyme inhibition assay for the treatment of Alzheimer disease. Curr Overv Pharm Sci. 2023; 4:98-107. https://doi.org/10.9734/bpi/cops/v4/4138C
4. Tukanatti B, Jadar P, Wasedar VS, Bhat K. Immuno-modulatory activity of *Mukta Bhasma* (calx of cultured pearls). Int J Ayurvedic Med. 2025; 16(2):422-429. https://doi.org/10.47552/ijam.v16i2.5389
5. Tukanatti PB, Jadar P, Vishwanath W. Hepatoprotective and anti-oxidant study of *Mukta Bhasma* (calx of cultured pearls) against CCl4-induced hepatic damage in rats (*in vivo*). Int J Life Sci Pharma Res. 2022; 12(5). https://doi.org/10.22376/ijpbs/lpr.2022.12.5.P34-40
6. Xu X, Liu L, Zhang W, Xu P. Effect of the water-soluble matrix of nanometer pearl powder on the osteogenic differentiation of hFOB1.19 cells. Exp Ther Med. 2025; 31(1):8. https://doi.org/10.3892/etm.2025.13003 PMid:41220913 PMCid:PMC12598726
7. Chacherkar PA, Dwivedi SS, Chandankhede JD, Lanjewar SR, Giradkar GL, Sahu AA, *et al*. Unravelling pearls cure: Investigation of the anticonvulsant and antioxidant effects of standardized pearl extract. World J Biol Pharm Health Sci. 2024; 20(2):531-540. https://doi.org/10.30574/wjbphs.2024.20.2.0912
8. Zhu C, Southgate PC, Li T. Production of pearls. Goods and services of marine bivalves; 2018. p. 73-93. https://doi.org/10.1007/978-3-319-96776-9_5
9. Qureshi MA, Bano H, Parveen S, Lari HA. Pearl (Marwareed) and its preparations: Strengthened the specific immune system and useful in stress, depression, phobia and epidemic diseases - A review. World J Pharm Res. 2020; 9(5):2654-2660.
10. Saharan N, Chahal RK, Abhishek. A review study on ancient drug *Mukta*. J Ayurveda Integr Med Sci. 2025; 10(4):232-237. https://jaims.in/jaims/article/view/4267
11. Sornamariyammal I. *Thathukalin Vilakkamum Marunthu muraikalum*. Chennai: Amudha Nilayam; 2012.
12. Li X, Xu P, Cheng Y, Zhang W, Zheng B, Wang Q. Nano-pearl powder/chitosan-hyaluronic acid porous composite scaffold and preliminary study of its osteogenesis mechanism. Mater Sci Eng C Mater Biol Appl. 2020; 111:110749. https://doi.org/10.1016/j.msec.2020.110749 PMid:32279810
13. Zhang S, Zhang T, Chen Y, Kourkoumelis N, Chen M, Dong J, *et al*. Pearl-like bioinspired coating enables regulation of Mg degradation for osteoporotic bone repair. Adv Sci (Weinh). 2025; e21927. https://doi.org/10.1002/advs.202521927 PMid:41420835 PMCid:PMC12955908
14. Formulary of India. The *Siddha* formulary of India. 1st ed. Vol. 1. Government of India Ministry of Health and Family Welfare; 1992.
15. Thiagarajan R. *Gunapadam thathu - Jeeva vagupppu*. 1st ed. Vol. 1. Chennai: Indian Medicine and Homeopathy Department; 2009.
16. Kannusamypillai C. *Sikicha Ratna Deepam*. Vol. 1. Chennai: Rathina Nayagar and Sons; 1951.
17. Sornamariyamal I. *Sarakku suthi Seimurai*. Chennai: Amudha Nilayam; 2012.
18. Jenifer VM, Jeylani MPAK. *Muthu Parpam*: Heavy metal analysis by ICP-OES. J Tradit Integr Med. 2022;5(2):473-476. https://jtim.biosci.in/ojs/index.php/jtim/article/view/111.
19. Chitra V, Sankaran V, Mahalakshmi V, Sugasini P, Samundeshwari P, Muthukumar NJ, Meenakumari R. *In vitro* antioxidant activity of *Siddha* herbomineral formulation *Muthu Parpam*. J Chem Health Risks. 2023; 13(6):458-465.
20. Yang HL, Korivi M, Lin MK, Chang HC, Wu CR, Lee MS, *et al*. Antihemolytic and antioxidant properties of pearl powder against 2,2'-azobis (2-amidinopropane) dihydrochloride-induced hemolysis and oxidative damage to erythrocyte membrane lipids and proteins. J Food Drug Anal. 2017; 25(4):898-907. https://doi.org/10.1016/j.jfda.2016.10.007 PMid:28987367 PMCid:PMC9328879
21. Jenifer VM, Jeylani MPAK, ShanthanaKumar M. Evaluation of anti-inflammatory activity of *Muthu Parpam* in Wistar albino rats. Int J Preclin Pharm Res. 2012; 13(1):5-7.
22. Chen Z, Yan Q, Zhang Z, Lan T, Liu P, Han S, *et al*. Immunomodulatory effects of Hydrolyzed Seawater Pearl Tablet (HSPT) on Th1/Th2 functionality in a mice model of Chronic Obstructive Pulmonary Disease (COPD) induced by cigarette smoke. Evid Based Complement Alternat Med. 2020; 2020:5931652. https://doi.org/10.1155/2020/5931652 PMid:33281913 PMCid:PMC7688355
23. Chen G, Chen H, Chen Z, Zhang M, Jiao Y, Wang Q, *et al*. The regulatory roles of choline in the immune response induced by LPS and transplantation in pearl oysters *Pinctada fucata martensii*. Aquac Rep. 2025; 45:103222. https://doi.org/10.1016/j.aqrep.2025.103222
24. Li YC, Chen CR, Young TH. Pearl extract enhances the migratory ability of fibroblasts in a wound healing model. Pharm Biol. 2013; 51(3):289-97. https://doi.org/10.3109/13880209.2012.721130 PMid:23043617
25. Li Z, Ur Rehman I, Shepherd R, Douglas TEL. Generation of pearl/calcium phosphate composite particles and their integration into porous chitosan scaffolds for bone regeneration. J Funct Biomater. 2024; 15(3):55. https://doi.org/10.3390/jfb15030055 PMid:38535248 PMCid:PMC10970912

26. Xia M, Huang D, Tong Y, Lin J. Pearl powder reduces sleep disturbance stress response through regulating proteomics in a rat model of sleep deprivation. J Cell Mol Med. 2020; 24(9):4956-4966. https://doi.org/10.1111/jcmm.15095 PMid:32220128 PMCid:PMC7205811
27. Chitra V, Rayma KR, Mahalakshmi V, Muthukumar NJ, Akila M, Thayalini K, *et al*. Evaluation of anti-cataract activity of the *Siddha* formulation *Muthu Parpam* using isolated goat lens model. J Adv Zool. 2024; 45(2):3992. https://doi.org/10.53555/jaz.v45i2.3992
28. Chen X, Peng LH, Chee SS, Shan YH, Liang WQ, Gao JQ. Nanoscaled pearl powder accelerates wound repair and regeneration *in vitro* and *in vivo*. Drug Dev Ind Pharm. 2019; 45(6):1009-1016. https://doi.org/10.1080/03639045.2019.1593436 PMid:30950303
29. Raghavi M, Karpagambal R, Subathra T, Abarna B, Shanmugapriya P, Madhavan R. Anticancer activity of *Siddha* formulation *Muthu Chenduram* against cervical cancer: An *in vitro* study. Int J Zool Investig. 2024; 10:372-378. https://doi.org/10.33745/ijzi.2024.v10i02.035
30. He W, Xu J, Zhao J, Wang Z, Kong R, Zhao F, *et al*. A multifunctional pearl powder-incorporated scaffold for bone regeneration: Simultaneous enhancement of osteogenesis, immune modulation, and angiogenesis. Biomaterials. 2026; 331:124086. https://doi.org/10.1016/j.biomaterials.2026.124086 PMid:41723902
31. Baines DK, Rachuna J, Hnydka A, Michalak A, Douglas TEL, Klimek K. Preliminary preclinical evaluation of innovative bone scaffolds composed of natural sources-whey protein isolate and pearl powder. Int J Mol Sci. 2025; 26(16):7939. https://doi.org/10.3390/ijms26167939 PMid:40869260 PMCid: PMC12386570

Author Contribution

Conceptualisation: Sasikumar Palanivel; Data collection and compilation: Sasikumar Palanivel; Manuscript Writing: Sasikumar Palanivel; Proofreading and editing: Sasikumar Palanivel, Amala Hazel Amaladason Mary Alphonsal, Mahalakshmi Varadhan, Manikgantan Erulandy Muthiah, Amudha Palanivelu. All authors have read and agreed to the published version of the manuscript.