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SHORT REVIEW

Review of *Siddha* Marine Drug - *Muthuchippi* (Pearl Oyster Shell) for Various Medicinal Properties

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Abstract

The *Siddha* system of medicine uses an opulent source of plants, metals, minerals, and marine and animal products for the preparation of medicine. The pearl oyster shell is a bivalve mollusc that lives in fresh and saltwater and generates pearls. The three major structural components of pearls are oblong, conchiolin, and calcium carbonate (CaCO3). Recently, interest in developing medications from marine materials has surged. In the fields of cancer, pain, and inflammation, many marine natural compounds are presently undergoing clinical trials. Pearl oyster shell, also known as *Muthuchippi*, is a key sea-derived medicine in the *Siddha* system of medicine. These shells include iron oxide, alumina, silica, calcium carbonate, phosphate, and sulfate of calcium and magnesium. Since it has been specially recommended to improve the strength, nutrition, and vitality of weak patients as well as for palpitations, digestion, heart tonic, and appetizer, pearl oysters are important in *Siddha* medicine. Traditionally, the calcined pearl oyster shell has been used to treat musculoskeletal diseases, anorectal diseases, respiratory diseases, and gastrointestinal diseases due to their high calcium carbonate content. This study aims to review several papers on the therapeutic potential of pearl oyster shells in treating various ailments. A comprehensive search of multiple databases, including PubMed and Google Scholar, yielded several papers for evaluation. According to this study, pearl oyster shells are utilized to cure a wide range of illnesses in all traditional Indian medical systems. Yet, there is scanty scientific data to support the efficacy of numerous indications. To substantiate this significant drug in the research forum, additional *in-vitro* and *in-vivo* studies must be carried out.

Keywords: Calcium, *Muthuchippi*, Pearl Oyster Shell, *Siddha* Marine Drug, *Siddha* Formulations, Traditional Medicine

1. Introduction

Pearl oyster shell is a bivalve mollusc of the *Pteridaea* family. The oysters are cultured for food and pearl production, and their shells are hard, rough, brown, or grey externally while being white, smooth, and shining internally[1]. It is composed of 95% calcium in the form of calcium carbonate and aragonite[2]. The shell has three layers: the outer periosteum layer with rich protein content, the medial prismatic layer with calcite crystals, and the inner nacreous layer with aragonite crystals[3]. The *Siddha* system of medicine, an ancient Dravidian culture, utilizes plants, animals, minerals, metals, and marine products to treat various ailments[4]. One of the *Siddha* marine drugs is pearl oyster shell (*Muthuchippi*)[4]. Pearl oyster shell is the origin of Pearl and has similar properties to Pearl in treating several diseases. In *Siddha* philosophy, Pearl is likened to Goddess Parvathi's power and is believed to possess lunar energy[4]. Pearl oyster shells are used in place of the pearl. It has been widely used in the *Siddha* system for the treatment of bronchitis, asthma, osteoporosis, nervous disorders, and musculoskeletal disorders[4,5]. It has a bitter taste and is used as a stimulant, stomachic, and nutrient[4]. Scientifically, various formulations using pearl oyster shell (*Muthuchippi)* were proven to have anti-microbial[6,7], anti-inflammatory[8], anti-peptic ulcer[9,10], anti-ageing[11], anti-cancer[12], and antioxidant

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activity[6]. The current article focuses on reviewing and explicating the medicinal value of pearl oyster shells (*Muthuchippi*) from various literature sources. It is bitter in taste and stimulant in action.

2. Overview

2.1 Vernacular Names[13]

Tamil: *Muthuchippi*
English: Pearl oyster shell
Sanskrit: *Muktashukti*
Hindi: *Motisimp*

2.2 Description of *Muthuchippi*

Pearl oyster shell (*Muthuchippi*) is procoline, equilateral, typically rounded anteriorly obliquely ovate in outline. It is a bivalve mollusc with three layers; the inner layer is the nacreous layer which produces pearls. This layer is known as the mother of Pearls. The second layer is the medial prismatic layer, and the outer layer is the perioscatrum layer[13].

2.3 Morphology of Oyster Shell

All oyster shells have a common morphology. There are three layers to the shell.

2.3.1 Periostracum

The outermost layer, the periostracum, is a thin, transparent, and delicate horny layer that allows the underlying colour to show through. It's easily worn off in old shells and extends beyond the calcareous material at the shell's free margin, where it's secreted by the mantle edge ectoderm cells[13].

2.3.2 Prismatic Layer

The middle layer, composed of calcareous prisms or columns, displays a cellular structure with a polygonal cross-section. As the shell grows, new prismatic layers form and fuse, one on top of the other, each deposited by the mantle epithelium near the free edge of the shell[13].

2.3.3 Nacreous Layer

The innermost nacreous or mother-of-pearl layer is composed of numerous fine lamellae of aragonite crystals[13].

2.4 Types of Muthuchippi

Pinctada and *Pteridaea* are two major families in India it is represented in Table 1.

Table 1. Representing the types of pearl oyster shell

Pinctada margaritifera	Black lip pearl oyster
Pinctada maxima	Gold-lipped or Silver lipped pearl oyster
Pinctada fucata	Akoya pearl oyster
Pinctada mazatlantica	Mazatlan pearl oyster or Panama pearl oyster
Pinctada albina	Shark Bay Pearl Oyster
Pteriia penguin	Penguin shell oyster
Pinctada radiata	Atlantic pearl oyster or gulf pearl oyster
Pinctada vulgaris	Indian pearl oyster

2.5 Distribution

2.5.1 Pinctada margaritifera

This species is mainly used in the *Siddha* system of medicine due to its vast availability in Indo-pacific regions such as the Red Sea, Arabian Sea, The Persian Gulf, India, Sri Lanka, Southeast Asia, Southern Japan, Australia, Madagascar, New Caledonia, Polynesia, Micronesia, New Guinea, Hawaii, Cocos – keeling island[13] (Figure 1).



Figure 1. *Pinctada margaritifera.*

2.5.2 *Pinctada maxima*

This species is distributed in the Indo-Pacific region from Myanmar to the Solomon Islands including Southern Asia, The Philippines, the South China Sea, and Australia[13] (Figure 2).



Figure 2. *Pinctada maxima.*

2.5.3 *Pinctada mazatlantica*

This species is found along the Western coasts of America extending from the Gulf of California to Northern Peru, including Baja California, Baja California Sur, Golfo de California, Isla Del Coco, and the West coast of Mexico, Panama, Coast Rica, and Ecuador[13] (Figure 3).



Figure 3. *Pinctada mazatlantica.*

2.5.4 *Pinctada albina*

This species is distributed to Northern Australia, from Indonesia through the Philippines up to Micronesia, China, Korea, and Vietnam[13].

2.5.5 *Pteriia penguin*

This species is distributed in the Red Sea and Arabian Gulf throughout the tropical eastern Indopacific to Southern Japan and Queensland round to Northwest Australia, Thursday Island, Southern China, and Taiwan[13].

2.5.6 *Pinctada fucata*

In India, it is found in the Gulf of Kutch, Gulf of Mannar, Palk Bay, Tamil Nadu, Andhra Pradesh, Kerala, and Karnataka[13] (Figure 4).

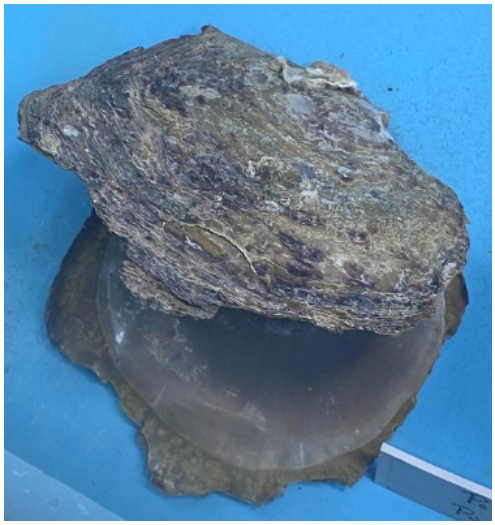


Figure 4. *Pinctada fucata.*

3. Literature Review

The review process is described in Figure 5.

3.1 Scientific Validation of Oyster Shell

X-RD analysis of pearl oyster shell: Oyster shells have a higher CaCo3 of 95.9% and a trivial amount of other ingredients (SiO2 (0.696%), MgO (0.649%), Al2O3 (0.419%), SrO (0.33%), P2O5 (0.204%), Na2O (0.984%), and SO3 (724%)). The particle size, bulk density, and apparent density were 1.65mm, 1.152g/cm^3 and 2.56g/cm[3,18].

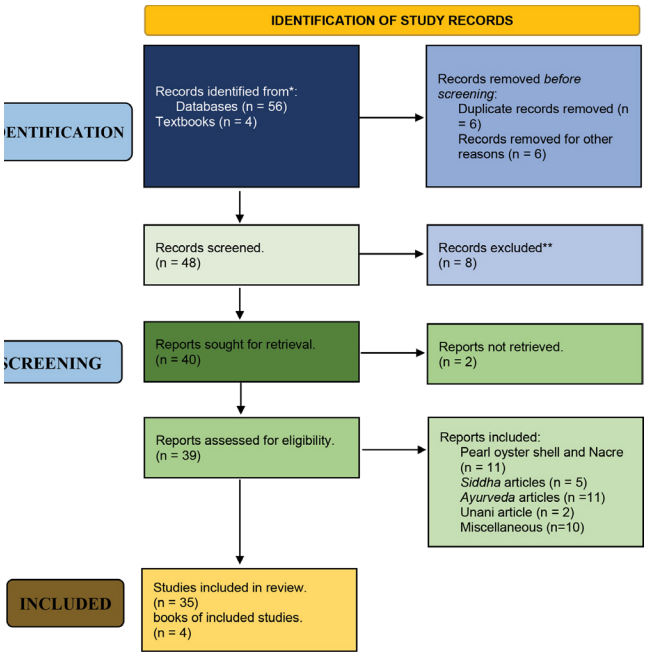


Figure 5. Prisma flowchart representing the study[17].

Nacreous layer of pearl oyster: The nacreous extract of pearl oyster shell for the treatment of depression and anxiety induced by lipopolysaccharide in mice, which showed improvement in behaviour and prevented oxidative stress by increasing the expression of nuclear factor E2-related factors. LPS injury causes decreased brain-derived neurotropic factor, which was reversed by treatment with nacre extract powder[19].

A study demonstrated that the nacreous layer attenuates amyloid beta-induced memory impairment via in vivo studies and found that it helps in the protection of hippocampus neurons by suppressing tau phosphorylation and AchE activity with an increase in the expression and phosphorylation of CREB[20].

Additionally, scopolamine-induced brain damage in rodents (Wistar rats and ICR mice) with Phosphate-Buffered Sulphate (PBS) as a control found that the damage can be reversed by the nacreous layer by reversed mRNA expression of Brain-Derived Neurotropic Factor (BDNF) and homer protein homolog in the hippocampus[21].

Also, the above study was further developed to isolate memory-improving substances using ion-exchange column chromatography and reverse phase column chromatography to elucidate the molecular mechanism underlying its memory-improving activity from a Sulphated polysaccharide which showed an increase in the expression level of antioxidant enzymes like copper and zinc. The study strongly suggests that the polysaccharide in the nacre extract mediated its anti-amnesic effects by preventing oxidative stress and inflammation and increasing the expression levels of BDNF and NGF[22].

3.1.1 Anti-aging Activity

The anti-ageing effect of nacreous layer extract from pearl oyster shells on D-galactose-induced brain and skin ageing was studied. This study showed that the nacreous layer extract suppressed ageing by up-regulating the expression of catalase and superoxide dismutase[11].

3.1.2 Anti-cancer Activity

The anticancer activity of oyster shells against oral cancer was conducted *in vivo*. The study consisted of 126 mice divided into 4 groups (normal diet, oyster powder, oyster calcium, and oyster extract) by treating C57BL/6 mice with Nitroquinoline I-Oxide (NQO) 50 µg/mL for 16 weeks, followed by normal water for 12 weeks, and treating with the study drug for 28 weeks. The tongue tissues were then assessed for histopathological changes. The results showed that oyster calcium samples showed a decrease in Proliferating Cell Nuclear Antigen (PCNA) and an increase in differentiation markers including keratin, involucrin, filaggrin, and loricrin[12].

3.1.3 Oyster Shell for Osteoporosis

The osteogenesis activity of oyster shells by precipitation technique[23]. Similarly, another study described that mantle gene 4 from *P. fucata* enhances osteoblast differentiation activity in MC3T3-E1 cell lines[24]. Additionally, a study showed that nano-powdered pearl oyster shells are beneficial in the treatment of osteoporosis induced by ovariectomy *in vivo*[25].

3.1.4 Oyster Shell in the Field of Periodontology

A study on the conversion of pearl oyster shell powder as Hydroxyapatite in 30 guinea pigs grouped into 3 groups 10 in each as negative control, positive control, and Hydroxyapatite. Observation was done for 14 – 21 days then, assessed for osteoprotegerin (OPG) and bone morphogenetic protein (BMP_2) expression and

found that Hydroxyapatite from pearl oyster shells showed higher expression of OPG and BMP_2. Thus, proving the efficacy of the pearl oyster shell[26].

3.2 Study of Various *Siddha* Formulations

Calcined pearl oyster shell powder (*Muthuchippi parpam)* is a widely used medicine effectively used for the treatment of bronchitis, asthma, and degenerative disorders in regular practice. This formulation has undergone numerous studies to elucidate the effectiveness of the drug. The following are the studies undergone in the above-mentioned formulation.

3.3 Analysis of Calcined Pearl Oyster Shell

Research on elemental characterization and physicochemical properties of raw pearl oyster shell (*Muthuchippi)*, purified pearl oyster shell (*Muthuchippi),* and calcined pearl oyster shell powder (*Muthuchippi parpam)* was done. The mean weight reduced from 850g to 500g. The Geochemical analysis shows that raw and purified pearl oyster shells were amorphous with aragonite traces of magnesium. The qualitative tests show the presence of tannins, flavones, proteins, and sugar. The results of FTIR showed the absence of pure organic compounds. The SEM analysis showed the particle size reduced to the nanoparticle. The XRD analysis showed the crystalline nature of the drug[27]. Another study on comparative XRD analysis calcination transformed pearl oyster shell from aragonite-calcite mix to mostly calcite (96%), retaining crystalline structure[28].

3.3.1 Antioxidant Activity

The antioxidant activity of calcined pearl oyster shell powder was determined by various antioxidant assays. The reducing power of calcined pearl oyster shell powder was evaluated by the method of Oyaizu with standard BHT in three observations and the absorbance values were calculated and converted to BHT equivalent in mg/gm. This drug was shown to have 210μgBHT/ 1000μg of the drug[6].

ABTS radical cation decolourization assay was done for different concentrations of Calcined Pearl oyster shell powder and absorbance was read at 745nm along with gallic acid standard and the observed value was 69.18% and 90.72% respectively[6].

3.3.2 Anti-microbial Activity

The antibacterial and antifungal activity of aqueous extract of calcined pearl oyster shell powder against bacteria (*E. coli* – 6.25, *Pseudomonas aeruginosa* – 12.5, *Kleibseilla pneumoniae* – 3.125, Salmonella typhimurium – 3.125, *bacillus subtilis* -<1.56) and fungus (*Aspergillus Niger* – 12.5, *Aspergillus fumigatus* – 25 and *Aspergillus flavus* – 12.5) which showed higher antifungal activity of calcined pearl oyster shell powder[6]. Also, another study on the antimicrobial properties of calcined pearl oyster shell powder against gram-positive bacteria including *Staphylococcus aureus, Staphylococcus saprophyticus, Staphylococcus pneumoniae, Bacillus substillis*, gram-negative bacteria including *Salmonella paratyphi*, *Salmonella typhi*, *shigella dysenteriea*, *Escherichia coli*, *Klebsiella oxytoca, P.* fluorescence, *Citrobacter* and *Acinetobacter* and yeast like *Candida albicans*. This study showed the highest zone of inhibition for yeast species at 50mm and the lowest inhibition for Citrobacter at 13mm, thus proving the anti-microbial activity of calcined pearl oyster shell powder[7].

3.3.3 Nephroprotective Activity

An *in-vivo* study was conducted to assess the nephroprotective activity in thirty Wistar rats, divided into 5 groups of 6 in each (I – Control 2% Sodium CMC for 14 days; II – single dose of Cisplatin; III – 5ml cystone syrup for 14 days with a single dose of Cisplatin; IV – 250mg/kg; V – 500mg/kg). The results found that calcined pearl oyster shell powder with Cisplatin treated rats had normal BUN after the intraperitoneal model of Cisplatin administration whereas the Cisplatin with 2% CMC treated rats had abnormally high BUN. The cystone-treated rats showed moderate BUN levels. Cisplatin-treated rats showed a marked reduction in weight with reduced GFR and increased BUN Level. Calcined Pearl oyster shell powder 500mg/kg showed a significant increase in body weight and increased urine output[29].

3.3.4 Clinical Study of Comparative Wound Healing Activity

A comparative clinical study was carried out to assess the topical wound healing activity of *Mathan thailam* and calcined cowrie shell powder (*palagarai parpam*

- MTP), *Mathan thailam* (MT), *Mathan thailam* and calcined pearl oyster shell powder(*Muthuchippi parpam* - MTM), in 6 cases of chronic non-healing lower extremity ulcers for 6 weeks and compared using leg ulcer measurement score before and after the treatment, which pursued the effectiveness of MTM in the treatment. The study results show that the MTM showed satisfactory improvement in treating chronic non-healing ulcers[30].

3.3.5 Clinical Study on Calcined Pearl Oyster Shell Powder for Renal Diseases

An open clinical trial was conducted on 20 patients with renal failure, administering *Mukirattai chooranam* (1g twice daily with hot water) and calcined pearl oyster shell powder (*Muthuchippi parpam* - 130mg twice daily with moringa leaf juice). The study revealed a significant decrease in serum creatinine, blood urea, and BUN levels before and after treatment. Additionally, there was a notable increase in GFR in all patients, and urine creatinine clearance levels also showed a significant improvement. The study concluded that the combination of both drugs is effective in treating renal failure[29].

3.4 Study of Various *Ayurvedic* Formulations

In *Ayurveda*, pearl oyster shell is used in various formulations viz, *Muktashukti pishti* and *Mukta Shukti Bhasma.*

3.4.1 Standard Manufacturing Process of Muktashukti Bhasma

A study was attempted to develop a Standard Manufacturing Procedure (SMP) on calcined pearl oyster shell (*Muktashukti Bhasma*) and calcined shell (*Jalashukti Bhasma)* by preparing five batches of each and comparing the expenses of the formulation. During the manufacturing process temperature of heat produced, weight loss during each step of the procedure, and quantity of juice used for triturating were recorded. The results obtained were found to be that the average temperature of pudam was observed as 859.80 and 852.6 for calcined shell in 1st and 2nd pudam respectively, and 850.80 and 849.2 for calcined pearl oyster shell in 1st and 2nd pudam, respectively. The average weight loss after purification was 12.08g for the calcined shell and 14.62g for the calcined pearl oyster shell. The average weight loss after the first pudam was 12.50g for calcined shell and 12.74g for calcined pearl oyster shell, the observed weight loss in the second pudam was 12.50g and 13.28g for calcined shell and calcined pearl oyster shell, respectively. The parpam obtained was sieved in 120 mesh sieves. The above study concluded that calcined pearl oyster shell preparation was 2.8 times costlier than calcined shell[31].

3.4.2 Muktashukti Bhasma Analytical Study

The physical and chemical analysis of calcined pearl oyster shell (*Muktashukti Bhasma)* was studied. Three samples of calcined pearl oyster shells weighed 400g each and were subjected to a purification process and observed for average weight loss to be 5.60%. The purified pearl oyster shell was further processed by 3-layer incineration and observed for weight changes. The average weight loss was found to be 16.6%. The qualitative tests found that the obtained product was white, lusterless, odourless, tasteless, and smooth fine powder with a pH of 9.5, which is alkaline in nature. The iron and calcium content were assessed by AAS and found to be two. And 40.04%w/w. The ash value, acid insoluble as, water-soluble ash and loss on drying were 97.184, 0.131, 26.156, and 0.055, respectively. Namburi Phase Spot Test (NPST) showed an immediate appearance of pink colour with 50% fading of the colour in 24 hours[32].

Another article states that calcined pearl oyster shell was prepared in three batches to elucidate the standard operating procedure, and a qualitative assessment was also done. This study revealed that the raw pearl oyster shell was found to be in aragonite form, and it was changed to calcite form after the incineration process. The physicochemical analysis shows trace amounts of lead, mercury, cadmium, and arsenic in permissible limits. The SEM analysis showed raw pearl oyster shell has a particle size between 968.5nm – and 578.5nm. From the XRD results, the raw pearl oyster shell has unevenly scattered particles while in the calcined pearl oyster shell, the particles were rod-shaped, stable, and arranged uniformly. The EDAX results revealed that the calcium content was found to be increased from 43.87% to 48.55%. Thus, this study proved that the calcined pearl oyster shell is a nanomedicine[33]. Similarly, the

instrumental analysis of calcined pearl oyster shell was studied in distinct phases of preparation (Raw (MSB 0), intermediate 1(MSB 1), intermediate 2 (MSB 2), final product (MSB 3), and marketed sample (MSB m)) by using XRD, SEM, and FTIR. The obtained XRD analysis was found to be calcite form in MSB 0, in MSB 1 calcite is in calcium carbonate and calcium hydroxide form, MSB 2 shows calcite, minimum amount of calcium hydroxide and calcium oxide, and the final product MSB 3 showed only the presence of calcite in calcium carbonate form. FTIR also confirmed this by indicating the calcite in MSB 3 and the presence of calcium hydroxide in MSB 2 and 3 SEM analysis showed that the particle size of MSB 0, MSB 1, and MSB 2, were larger and un-uniformly arranged to MSB 3, it is lesser in size and uniformly arranged[34].

3.4.3 Namburi Phased Spot Test

Namburi phased Spot Test (NST) is a technique used for assessing the quality of a Herbo-mineral compound. NST in 3 different marketed samples (S1, S2, S3) with a control (C), prepared by classical method. The study observed that C and S2 were similar in colour and shape to standard whereas S1 and S3 showed a marked deviation of spot changes due to adulterated Calcined shell powder (*Shukti bhasma)*. Thus, the study concluded that the changes may be due to the usage of cultured pearl oyster shells instead of natural pearl oyster shells[35].

3.4.4 Muktashukti Bhasma as a Nanomedicine

Research was done to establish the uses of nanomedicine in the treatment of several diseases and nano-biology. The study also assessed 2 *Ayurvedic* formulations calcined pearl shell powder *(Muktashukti Bhasma)* and calcined gold (*Swarna Bhasma)* for SEM and TEM analysis to prove the availability of nanomedicine in *Ayurveda*. From this study, the SEM analysis showed calcined pearl shell powder *(Muktashukti Bhasma)* was found to be between 84.4nm - 123.4nm. The particle size of raw pearl shell powder was found to be reduced in calcined pearl shell powder *(Muktashukti Bhasma)*[36].

3.4.5 Anti-inflammatory Activity

The anti-inflammatory activity of calcined pearl shell powder *(Mukta Shukti Bhasma* (MSB)), an *Ayurvedic* formulation was done. Albino rats were induced oedema by sub-plantar injection of Carageenan, Histamine, 5HT, nystatin, and subcutaneous implant of cotton pellets. In all the above conditions MSB 100mg/kg was proven to exhibit the effect of the standard drug acetylsalicylic acid (ASA) of 300mg/kg. Rats pretreated with MSB delayed castor oil-induced diarrhoea by inhibiting the activity of prostaglandin. Thus, the MSB is found to be as potent as the standard drug ASA[8].

3.4.6 Anti-peptic Ulcer Activity

In *Ayurveda*, the pearl oyster shell is used to make a formulation named *Mukta shukti Bhasma* which is calcined pearl shell powder. The anti-peptic ulcer activity in 238 Albino rats of either sex in seven groups [control, 100mg/kg, 300mg/kg, 1000mg/kg, three groups as ranitidine 0.5mg/kg, 2mg/kg, 5mg/kg] was studied which exhibited a significant reduction in free and total activity. This also raises the pH levels[9].

3.4.7 Comparative Study of Bhasma on Anti-ulcer Activity

The effectiveness of calcium-based *Ayurvedic Parpam* (*Bhasma* - oxide) and *Chunnam* (*pishti* - Caustic) for the treatment of gastric ulcers was studied in Charles foster albino rats of 13 groups (n=6, 3 of each sex) by aspirin-induced gastric ulcer and ethanol-induced gastric ulcer. After 1hr of ulcer induction in pretreated rats, the gastric portion was excised and incised for assessing the ulcer index. The results exhibited that the calcined pearl oyster shell-treated rats showed 62.85% inhibition at 25mg/kg and 73.31% at 50mg/kg in Aspirin-induced gastric ulcers and 70.89% and 74.06% inhibition at 50mg/kg Ethanol-induced gastric ulcer which are comparatively higher than the standard drug ranitidine 50mg/kg (Aspirin-induced – 40.97%; Ethanol-induced – 56.60%). The ulcer index calculated was found to be 6.50±0.62, 4.67±1.54, and 10.33±1.23 respectively in Aspirin-induced ulcer pretreated with calcined pearl shell powder 25mg/kg, 50mg/kg, and ranitidine 50mg/kg. The ulcer index for ethanol-induced gastric ulcer was found to be 9.17±1.89, 8.17±2.04, and 13.67±1.89 respectively for calcined pearl shell powder 25mg/kg, 50mg/kg, and ranitidine 50mg/kg. Thus, this paper elucidates that calcined pearl

shell powder can be effectively given for the treatment of ulcers[10].

3.4.8 Toxicity Study on Muktashukti Bhasma

The acute and sub-acute toxicity of calcined pearl shell powder *(Muktashukti Bhasma)* was done. The acute toxicity in rats with a dosage of 5000mg/kg which is 3-10 times the normal prescribed dose. The study did not produce any toxicity. Sub-chronic toxicity in rats at a dose of 25mg/kg and 85mg/kg for 30 days, average changes in weight loss, food, and water intake were assessed in 0,20,30 days. At the end of the 30th day, animals were sacrificed and analyzed for haematological, and biochemical electrolyte concentration and histopathological changes were assessed. This study proved to be safe without producing any toxicity[37].

3.4.9 Clinical study on Muktashukti Bhasma

A prospective double-armed observational clinical study on 42 patients within the age group 45-65 years of osteopenia and osteoporosis without any co-morbidity was assessed, by administering *Laksha Guggulu* (500mg) and *Muktashukti bhasma* (250mg) BDS with lukewarm water, for 12 weeks (84 days) showed a significant increase in their quality of life (QUALIFFO-41) statistically, the p-value is less than 0.001. Thus, proving the efficacy of Calcined pearl oyster shell for treating osteoporosis[38].

3.5 Study on Unani Formulation

3.5.1 Chemical Characterization of Kusta-e-Sadaf

A study on physicochemical characterization of Calcined pearl oyster shells assessed the particle size as 20.5µm, bulk density, and tapped density as 0.918 and 1.268, respectively. The calcium carbonate content was assessed in the oyster shell (*Sadaf - Muthuchippi*) and Calcined pearl oyster shell (*kusta-e-Sadaf*) in two different methods viz, acid-base trituration and complexometric trituration, it was found to be 94.55%, 95.32% earlier and 98.81%, 99.55% in later. The calcium content was also assessed in the same method, which was found to be 34.69 %, 34.98% in oyster shells, 36.26%, and 36.53% in Calcined pearl oyster shells, respectively. ICP analysis reveals the permissible limits of mercury, cadmium, lead, chromium, and tin. The assessed microbial load and total aerobic count were under the limits[39].

3.5.2 Comparative Evaluation of Kusta-e-Sadaf of Various Origins

The Unani system of medicine uses pearl oyster shells for the treatment of several diseases one such formulation is *Kushta de Sadaf* i.e., calcined pearl oyster shell. A study compared the chemical composition, elemental analysis, and heavy metal content of calcined pearl oyster shell (*Kushta de Sadaf*) from different sources: traditional classical method, modern furnace method, and commercial market samples. The results revealed that the market sample contained heavy metals exceeding safe limits, while the furnace method sample had elevated lead levels beyond the permissible range[40].

4. Discussion

The marine ecosystem is a crucial source of bioresources for human health and an essential cradle of life. The diverse range of environments provided by various oceanic zones results in a vast array of creatures. Notably, ancient medical systems such as *Siddha* have been using these marine medicines long before the study into marine natural products began, approximately 50 years ago[41]. Almost 80% of all flora and fauna on Earth are marine species, which are also a rich source of new and potentially useful biomolecules[41]. The chemistry of marine animals is mostly unexplored while making up 79% of the surface of the planet. This presents a huge opportunity for developing novel medications to treat serious illnesses. Recently, a wide range of marine invertebrates and animals, including tunicates, sponges, soft corals, sea hares, nudibranchs, bryozoans, and sea slugs, have had several bioactive chemicals recovered from them[42].

Recent studies validate the fact that plain pearl oyster shells have high calcium content. Among the three layers of pearl oyster shell, the nacreous layer extract is proven to exhibit anti-ageing, anti-cancer, osteogenic, and neuroprotective activity. Calcined pearl oyster shell (*Muthuchippi parpam)* is a *Siddha* Herbo-Marine formulation that has been prescribed for decades and has proven its efficacy. Most marine-derived compounds have been scientifically revealed to have

antiviral and antifungal properties[43]. *In vitro* studies on the anti-microbial and antioxidant properties of the *Siddha* formulation calcined pearl oyster shell showed greater efficacy against fungal infections. Clinically, the calcined pearl oyster shell was found to exhibit wound-healing activity. The *Ayurvedic* formulation of calcined pearl oyster shell is proven to have anti-peptic ulcer activity and anti-inflammatory activity through in-vivo studies. Acute and sub-acute toxicity studies have been carried out and proven for its safety. The *Siddha*, *Ayurveda*, and Unani formulations of calcined pearl oyster shell powder were studied for biochemical analysis and instrumental analysis. According to this article, the pearl oyster shell can be used impeccably in treating various diseases including cancer. The calcined pearl oyster shell is of nanoparticle size which aids in easy absorption into the cells. The osteogenic activity of pearl oyster shells is due to the presence of calcium carbonate. Given the scientific data examined in this research, it is evident that calcined pearl oyster shell is an affordable medication for several of the conditions listed in the *Siddha* literature. Many studies have been done *in vitro,* yet clinical studies should be carried out for further study of its efficacy.

5. Conclusion

In the era of non-communicable diseases due to rapid lifestyle modifications, Pearl oyster shells (*Muthuchippi)* can be a promising source of treatment. While modern medicine recently has turned its focus on marine medicinal resources, in *Siddha*, marine species especially, calcined pearl oyster shells have been used for decades to treat a variety of illnesses like respiratory illness, musculoskeletal diseases, and gastrointestinal diseases. Moreover, several studies have already proven the scientific efficacy of the drug from pearl oyster shells. Toxicity studies and Randomized clinical trials need to be conducted to provide scientific proof of the importance of pearl oyster shell medicinal formulations and their clinical uses.

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