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(REVIEW ARTICLE)

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Unravelling pearls cure: Investigation the anticonvulsant and antioxidant effects of standardized pearl extract

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Abstract

The majority of people are aware of pearls, but their therapeutic benefits have not gained widespread recognition. This page summarizes pearls' 2,000-year medicinal history in China, including their use in traditional Chinese medicine and their many preparations, as well as the advancements in their chemical components, pharmacology, toxicology, and clinical research. In China, 251 prescription formulations and nine different nationalities employ pearls from three different sources as medical materials. Pearls also include a variety of organic and inorganic components, including amino acids and trace elements and calcium carbonate. Pearls are safe to consume for an extended period of time without causing any noticeable negative effects, according to toxicology. Clinically speaking, pearls have been used to treat a wide range of illnesses and ailments, including epilepsy, convulsions, palpitations, eye disorders, ulcers, skin disorders, and skin blemishes. This article serves as a resource for future pearl research and use.

Keywords: Pearls; Chemical Constituents; Pharmacology; Clinical Application; Pearl Powder; Nacre Powder; Extraction; Purification.

1. Introduction

The most popular and traditional gem is the pearl. They don't require polishing and were the first gemstones used by humans. The smooth, glossy, and multicolored deposits (nacre) that surround a grain of sand or other foreign material in the shells of some freshwater mussels and marine oysters make pearls extremely valuable biological gem stones. They are used in toothpaste and cosmetics and have therapeutic benefits in addition to being aesthetically pleasing.[1]

In addition to being a type of sea shellfish, pearls are used as traditional natural medicine. Inflammation, burns, scalds, wounds, cuts, and pain healing are just a few of the conditions that marine mussels have long been used to treat. Furthermore, pearls have important whitening, relaxing, and vision-improving properties. For thousands of years, it has been used as medicine in China, and many different ethnic groups have utilized it simultaneously. Among other conditions, epilepsy, eye disorders, and skin conditions have all been treated with pearls or pearls combined with other medications in recent studies.[2]

Since pearls are currently widely cultivated in many nations, the cost of perfectly round, glossy pearls for jewelry can be extremely costly, yet the cost of pearl powder for cosmetic and medical items is rather low.[3]

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Figure 1 Pearls

1.1. History

Pearls have captivated people since the beginning of time. Pear-shaped pearls are frequently found in nature. The Latin word 'pirula', meaning pear, is the source of the English term pearl. From the Sanskrit language, pearl is called 'Mukta', meaning purity. It is believed that natural pearls predate Christ by 3500 years. In addition to the Bible and Quran, these pearls were mentioned in the Indian Vedas and Puranas. The Rigveda and the Indian epics Ramayana and Mahabharata both make reference to pearls. In Hindu literature, Krishna, the eighth incarnation of Vishnu, is linked to the fictitious genesis of pearls. Chinese literature claims that pearls have been courted since 2200 BC.Following the discovery of pearls in Australia by British naturalist William Saville Kent, Toichi Nishikawa and Tatsumi introduced pearl growing techniques to Japan. In 1989, the Central Institute of Freshwater Aquaculture (CIFA) started growing pearls in freshwater. China, Japan, Australia, Indonesia, France, Cook Islands, Philippines, India, Sri Lanka, Bangladesh, Myanmar, Malaysia, and Mexico are among the countries in the globe that currently produce pearls for commercial use. The two countries that produce the most freshwater and marine pearls are China and Japan.[4]

In addition to being a type of sea shellfish, pearls are used as traditional natural medicine. Inflammation, burns, scalds, wounds, cuts, and pain healing are just a few of the conditions that marine mussels have long been used to treat. Furthermore, pearls have important whitening, relaxing, and vision-improving properties. For thousands of years, it has been used as medicine in China, and many different ethnic groups have utilized it simultaneously. Among other conditions, epilepsy, eye disorders, and skin conditions have all been treated with pearls or pearls combined with other medications in recent studies.[5]

1.2. Cultivation methodology

The surgical procedure carried out inside the pearl mussel's internal structure and the kind of pearl goods being targeted determine the variety of freshwater pearl subculture techniques. The most important component in pearl culture operations is a shell bead. In the freshwater pearl way of life, certain locally accessible, less expensive, and biocompatible acrylic fabrics can be used as nuclei. Pearl mussels with shell lengths of 8 to 10 cm and weights of 50 grams or more have been shown to be ideal for pearl production operations.

- Culture Practices:Collection of mussels, pre-operative conditioning, surgical treatment, post-operative care, pond culture, and pearl harvesting are the six crucial processes that make up the farming technique of the freshwater pearl culture operation.
- Collection of mussels:The healthy mussels grow in freshwater bodies such as ponds, rivers, and many more. They can be manually gathered and stored in water-filled buckets or containers. The ideal mussel length for the pearl way of life is more than eight centimeters from front to back.

- Pre-operative Conditioning:Pre-operative conditioning is used to weaken the adductor muscle tissue, which facilitates easier handling during surgery. The collected mussels are kept in captivity for two to three days in a crowded condition with aged tap water at a stocking density of one mussel/lit.[6]

1.3. Formation of pearls

The process of natural biomineralization yields pearls. A special biological synergy leads to biomineralization, the biological process by which an organism creates mineralized tissue. Pearl creation occurs when the defensive function of pearl clams or mussels is triggered by external stimuli, such as foreign items, and the top mantle envelops the foreign objects. A pearl sac is gradually formed by the invaginated portion of a single layer epithelial tissue's cells, which continuously secrete nacre on foreign objects. Nacre is still secreted by the pearl sac, which encloses it and eventually turns into a pearl.

There are two successive stages in the production of pearls. The first is the uneven deposition of CaCO3 on the exposed nucleus; the second is the gradual formation of a mature nacre on the nucleus, which is comparable to shell renewal. A number of genes and proteins, including the pearl shell matrix protein gene, are expressed and released throughout the two to three years it takes for pearls to form. Together, these genes and proteins control how pearls form, including their size, shape, and growth. The nacre layer, which contains the prismatic and aragonite layers, the amorphous matrix layer, and the pearl nucleus make up the majority of pearls. After being ground and polished, the pearl nucleus is a tiny ball that can be implanted artificially or spontaneously.[7]

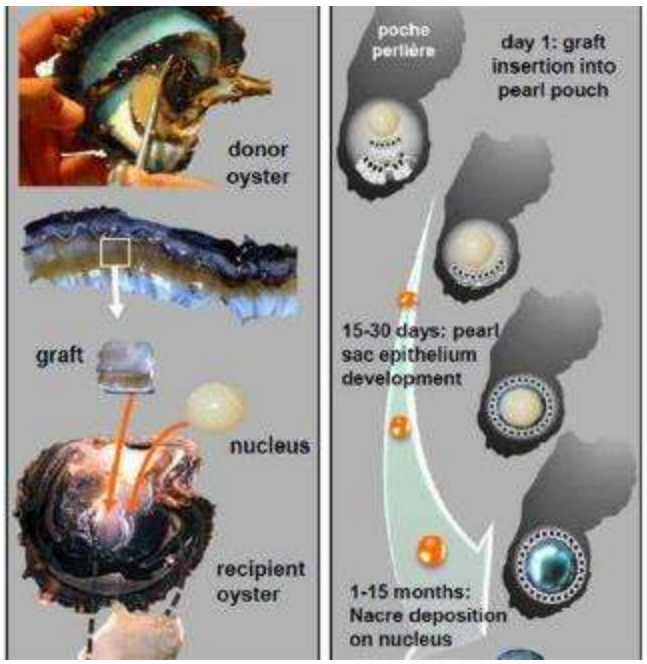

Figure 2 Formation of Pearls

Table 1 Origin of Pearls [8]

Country/Place	Species
India	*Lamellidens marginalis* *Parreysia corrugate* *Lamellidens corrianus*
China	*Cristaria plicata* *Hyriopsis cumingii* *Lamprotula tortuosa* *Hyriopsis schlegelii* *Lamprotula leai*

	Lanceolaria glayana
Bangladesh	*Lamellidens marginalis* *Lamellidens corrianus* *Lamellidens jenkinsianus* *Parreysia daccaensis* *Parreysia favidens*
Japan	*Hyriopsis schlegelii* *Margaritifera laevis* *Cristaria plicata* *Margaritiana dahurica*
Indonesia	*Anodonta woodiana*
Portugal	*Margaritifera margaritifera*
South Korea	*Cristaria plicata*
Vietnam	*Sinohyriopsis cumingii* *Cristaria bialata* *Sinanodonta elliptica* *Sinanodonta woodiana* *Lamprotula leai*
Mexico	*Psoronaias crocodilurum* *Potamilus alata*
Nepal	*Lamellidens marginalis*
North America	*Quadrula sp.*

1.4. Chemical constituent of pearls

Mollusc shells are mostly composed of calcium carbonate ($CaCO_3$) and magnesium carbonate, with proteins, glycoproteins, and polysaccharides making up the remaining organic matrix.[9]

Silica, calcium phosphate ($Ca_3 (PO_4)_2$), aluminum oxide, and iron oxide make up the remainder of the shell. Additionally, trace amounts of copper, manganese, selenium, aluminum, and sodium are found in pearl. Pearl powder has been shown in animal experiments to have positive pharmacological effects, including anti-oxidant, anti-inflammatory (since it contains magnesium), and anti-aging (by stimulating fibroblasts), immunomodulating, and wound healing. [10,11] As a result, pearl powder has been included into nutritious diets and used to treat duodenal, stomach, and aphthous ulcers.[12]

There are also essential amino acids with antioxidant qualities that may strengthen the immune system, such as glutamate (Glu) and aspartate (Asp).[13,14]The antioxidant qualities of pearl powder are further enhanced by the hydrophobic amino acids cysteine (Cys), isoleucine (Ile), leucine (Leu), methionine (Met), phenylalanine (Phe), tryptophan (Trp), and valine (Val), which also have strong free radical quenching potential [15]. By serving as cofactors for antioxidant enzymes, calcium, magnesium, and selenium give pearl powder its antioxidant properties.[16]

Table 2 Chemical Constituent

Content	**%concentration**
$CaCO_3$	90%
Water	2 to 4%
Organic matter	3.5% to 5.9%
Other substances	0.1% to 0.8%

1.5. Calcium Carbonate

Molecular formula: $CaCO_3$

Molecular weight: 100.0869 g/mol

Solubility: Very low solubility in pure water (15mg/L at 25°C)

Melting point: 825°C

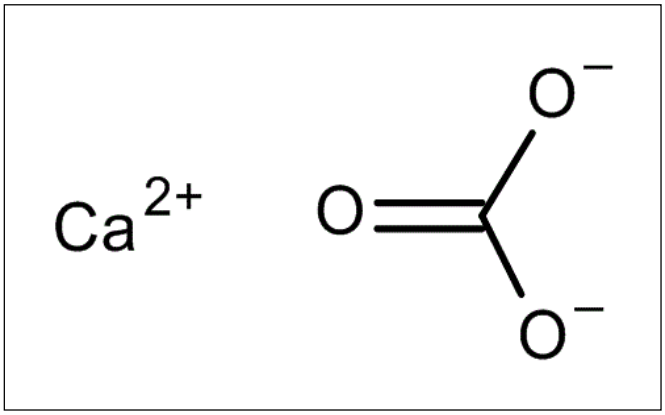

Figure 3 Structure of calcium carbonate

Table 3 Characteristics of pearls [17]

Sr. No.	Parameter	Characteristics
	Category	Carbonate mineral, protein
	Chemical Formula	$CaCO_3$
	Crystal System	Orthorhombic
	Colors	 White Cream Grey Blue  Black Dark grey Green Purple  Pink Golden

	Hardness	2.5 – 4.5 on the Mohs scale
	Refractive Index	1.52 – 1.66
	Specific Gravity	2.60 – 2.85
	Birefringence	0.156
	Luster	Pearly
	Cleavage	None
	Fluorescence	White pearls: light blue to light yellow; golden pearls: yellow-green to dark brown; black pearls: commonly pink to orange-red

2. Pharmacological effects and partial mechanism of action of pearls

2.1. Anti-Epileptic Effect

The intracerebral excitatory neurotransmitter 5-hydroxytryptamine (5-HT) and the inhibitory neurotransmitter γ-aminobutyric acid (GABA) are linked to various kinds of seizures. Pentylenetetrazole-induced epileptic convulsions resulted in downregulated $GABA_B$ levels and elevated 5-HT3 expression. The expression of 5-HT3 and the level of $GABA_B$ were somewhat restored following treatment with the original pearl powder, pearl water-soluble protein, pearl acid-soluble protein, and pearl conchiolin protein; the protein extracts showed the most notable impact. This suggests that the active ingredients causing the anti-epileptic action might be proteins.[18]

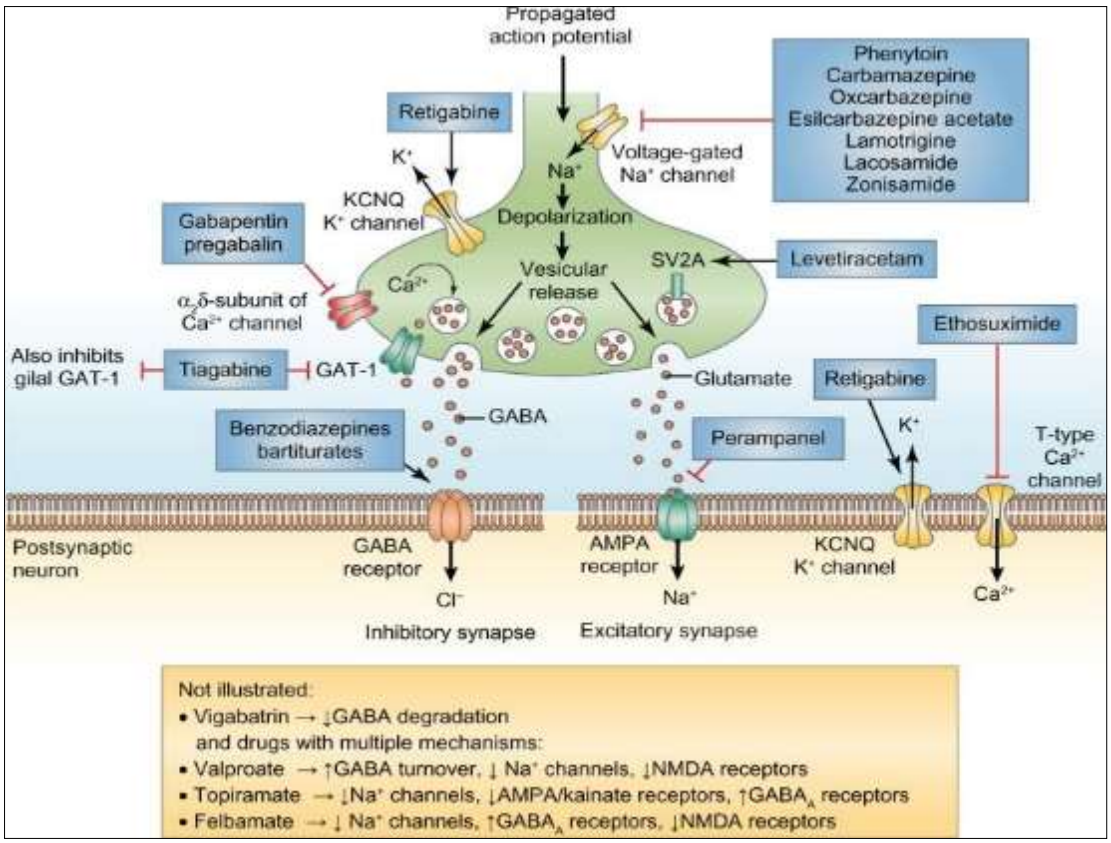

Figure 4 Mechanism action of Anti-Epileptic

2.2. Anti-Oxidative Effect

SOD and glutathione peroxidase (GSH-Px) would inhibit the oxidative process, while the presence of (1,1-diphenyl-2-picrylhydrazyl) radical (DPPH·), 2,2′-azinobis (3- ethylbenzothiazoline-6-sulfonic acid) radical (ABTS·), hydroxyl radical (OH·), and superoxide anion radical (O_2- ·) would exacerbate the oxidation reaction.

It has been demonstrated that pearls are a great antioxidant. The DPPH and ABTS· free radicals were strongly scavenged by seawater pearl hydrolysate and freshwater pearl hydrolysate, while OH· and O_2-· were comparatively weakly scavenged. However, the concentration of pearl hydrolysate employed was significantly lower than that of ascorbic acid at an identical scavenging rate, and the scavenging rate of all free radicals rose as the volume fraction of pearl hydrolysate increased.Furthermore, DPPH· and O_2-· were scavenged by pearl powder, protein extracts in pearl powder, and non-protein extracts in pearl powder. The scavenging ability of protein extracts was greater, suggesting that the protein composition of pearls may influence their antioxidant capacity. However, a study revealed that the pearls' (macroporous resin) early purification protein sample exhibited a good scavenging ability for OH but no discernible scavenging ability for DPPH· and O_2-·. The procedure used to extract pearls may be the cause of the disparate outcomes stated. Furthermore, the effective protein has not been shown, and the initial purified protein sample might only be a portion of the entire protein.

Pearl extracts can scavenge free radicals in place of SOD because of their SOD-like impact on oxidative enzymes. In medium-aged rats, pearl hydrolysate can lower lipid peroxide production and increase SOD activity. In vitro tests further demonstrated that pearl hydrolysate can lower glutathione, lower malondialdehyde, scavenge active free radicals, protect cells from H_2O_2-induced oxidative damage, and increase GSH-Px activity in human lens epithelial cells and microvascular endothelial cells. Additionally, antioxidants contribute to a longer lifespan. It was demonstrated by Huang and Pan (2000) and Ma and Xiao (2007) that giving Drosophila pearl powder at an early age could increase its vitality.The aforementioned illustrates how enzyme activity can impact free radical scavenging, suggesting that the oxidation process is a chain reaction. Therefore, more investigation is required to fully understand pearl powder's antioxidant mechanism. [19]

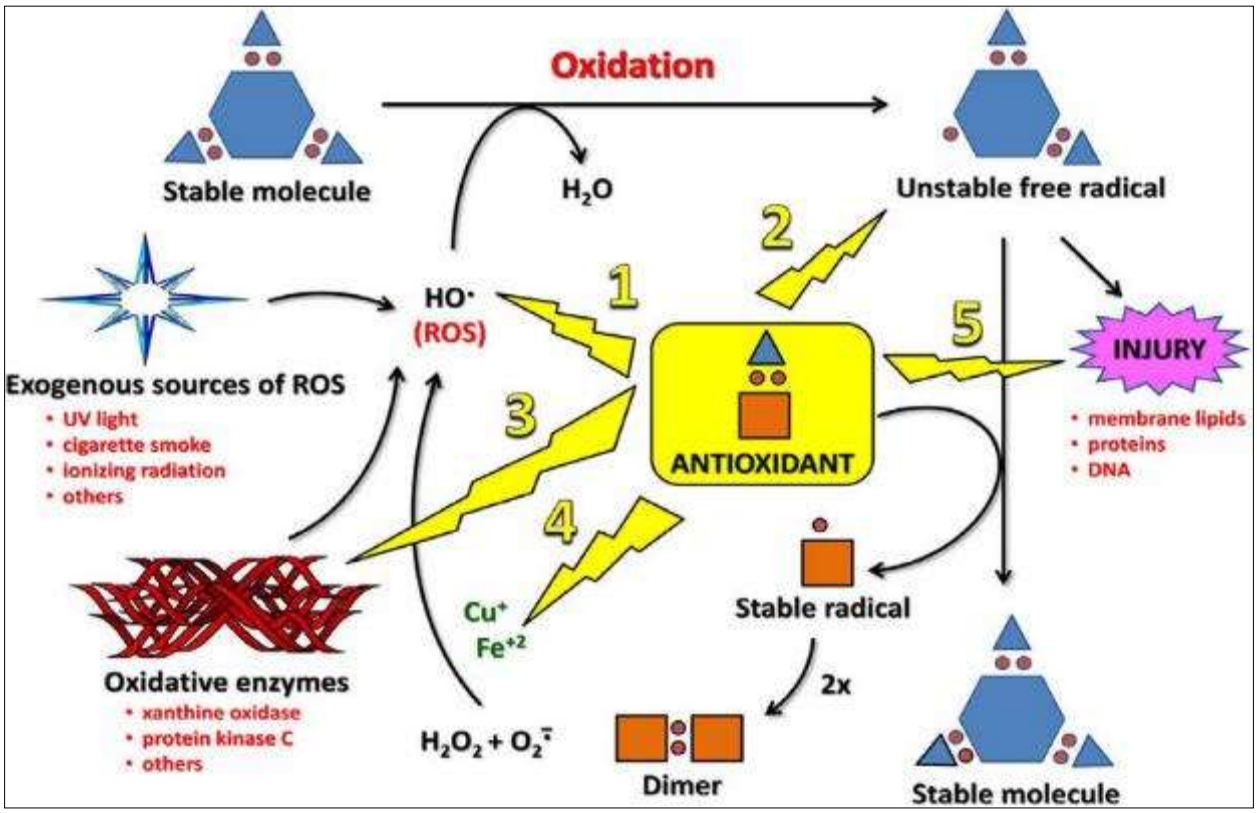

Figure 5 Mechanism action of Anti-Oxidant

2.3. Other applications of pearls

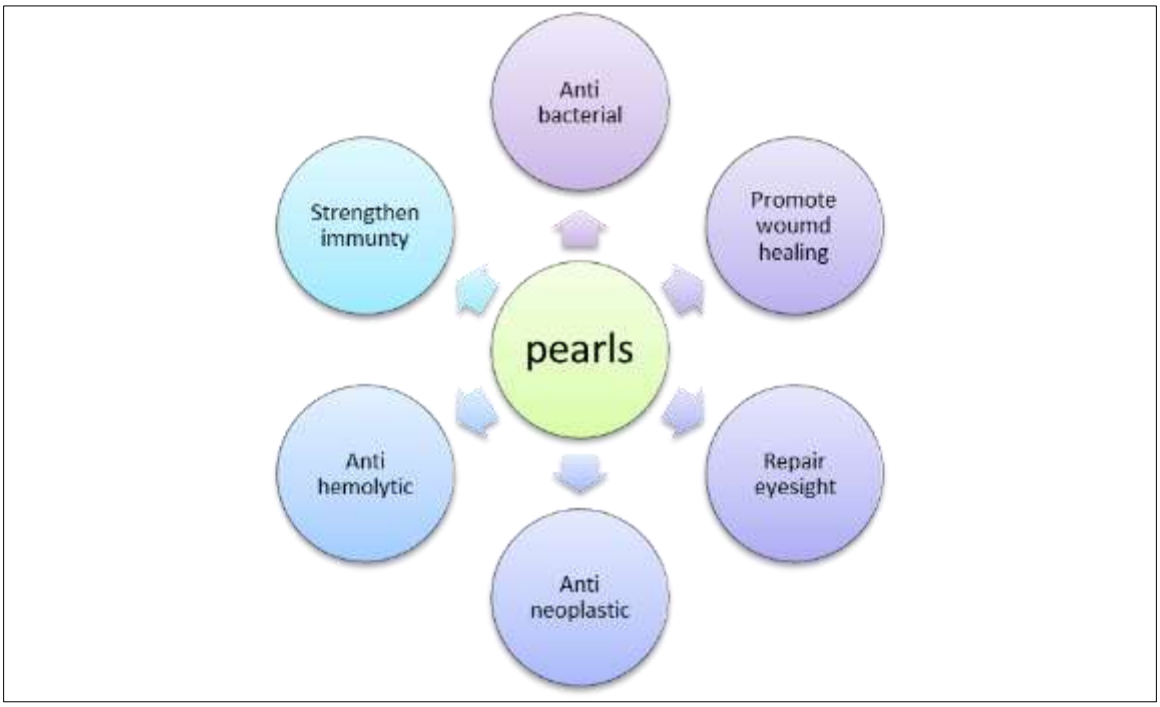

Figure 6 Other Application of Pearls

3. Materials and methods

3.1. Preparation of pearls powder

Ten kilograms of pearl were prepared, cleaned with purified water, and screened to get rid of stones, sand, and other solids.

The cleaned pearl was immersed in stale soybean milk made with a 1:10 soybean to water ratio for over 72 hours, until the milk level covered the entire pearl. The stale soybean milk was then poured out, and the pearl was cleaned with a lot of water to get rid of the bad odour before being heated to dryness.

The dry pearl was crushed into a superfine powder using a 300-mesh crushing machine wash.

The resulting fine pearl powder was placed in a mixer with almost ten times as much water added. The mixer was then begun to mix the fine pearl powder and water at 1000 r.p.m. for over ten minutes before stopping.

After the suspension had been removed from the mixer using a 1000 mesh screen, water was added, and the process was repeated.

All of the pearl powder suspension that made it through the 1000 mesh filter was gathered and dried at 18°C to create pure pearl powder, which weighed 6 kg and represented a 60% harvesting rate. The resulting pure pearl powder was measured to have a grain diameter of 50–100 nm.

The resulting pure pearl powder's heavy metal composition reveals that the levels of arsenic, lead, and mercury are 2.28 ppm, 0.36 ppm, and 0.62 ppm, respectively: When untreated pearl is crushed directly into pearl powder using a 300-mesh crushing machine, the resulting powder's arsenic, lead, and mercury concentrations are 5.26 ppm, 117.63 ppm, and 3.89 ppm, respectively.

3.2. Preparation for pills for anti-epileptic action:

Take Pearls powder and mix withHeartwood of Santalum album,Heartwood of Dalbergia odorifera,nine ocular stones (a mineral gem),Stigma of Crocus sativus,Gallstones of Bos taurus domesticusArtificial secretionsin male sachets of Moschus berezovskii or Moschus sifanicus or Moschus moschiferus.

- Add all ingredient and mill to together with thw the help of grinding process.
- After that pass all the powder through by sieve for ensure particle uniformity.
- Then form granules from powder i.e. wet granulation/ dry granulation.
- Then filling die cavities with granules.
- Allow the compression on it to form pills and eject from it.
- After that pills are obtained and coating can be done if needed.

4. Challenges and Overcome

4.1. Pearl Formulation Challenges

- Stability and Shelf-Life: Maintaining pearl's stability and shelf-life in various environmental conditions.
- Bioavailability: Ensuring optimal bioavailability of pearl's nutrients.
- Taste and Odor: Masking unpleasant taste and odor of pearl.
- Particle Size: Controlling particle size for optimal absorption.
- Interactions: Potential interactions with other ingredients or medications.
- Cost-Effectiveness: Balancing formulation costs with market pricing.

4.2. Pills Formulation Challenges

- Bioavailability: Ensuring optimal bioavailability of active ingredients.
- Tableting: Overcoming tableting challenges (e.g., compression, hardness).
- Disintegration: Controlling disintegration time and rate.
- Coating: Applying effective coatings for controlled release.
- Fillers and Excipients: Selecting optimal fillers and excipients.

4.3. Common Challenges

- Quality Control: Maintaining consistent quality.
- Scalability: Scaling up production while maintaining quality.
- Regulatory Compliance: Meeting regulatory requirements.
- Consumer Acceptance: Ensuring consumer acceptance and satisfaction.

5. Conclusion

For the first time, this research provides a thorough explanation of the medicinal history of pearls in China, as well as their chemical makeup, pharmacological influence on epilepsy, and therapeutic use. Research on the chemical components of pearls as a natural mineral medicine has several limits; it is unknown which individual compounds are useful. The majority of them make use of extracts, including enzymatic hydrolysis, acidolysis, and water extraction. Protein extracts have a greater effect than the others, yet frequently, a single extraction will result in the loss of numerous useful components. Therefore, in order to improve the curative impact, it is frequently essential to combine several extracts. More research is required to determine the precise active ingredients. Proteomics is a novel research technique that can be utilized to investigate the precise active ingredients of protein-containing pearls. Although the majority of pearls' pharmacological effects have been established, most of them just exist on the surface, and more research is needed to fully understand the mechanism. Pearls are mostly utilized in clinical settings in conjunction with other medications to treat illnesses. Although there aren't many examples of pearls being used alone to cure illnesses, this may make it impossible to provide concrete evidence of pearls' efficacy. Nevertheless, these clinical trials are still somewhat significant as references. In summary, pearls have a lot of potential for development, and more people ought to be aware of their therapeutic benefits. We should concentrate on the development of pearls in the future in two ways: first, to encourage the identification of additional active components in pearls, and second, to establish the groundwork for their clinical use.

Compliance with ethical standards

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Disclosure of conflict of interest

No conflict of interest to be disclosed.

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