Review Article

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PHARMACEUTICS, ETHNOPHARMACOLOGY, CHEMISTRY AND PHARMACOLOGY OF AYURVEDIC MARINE DRUGS: A REVIEW

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ABSTRACT
Ayurveda is the ancient thought and treatise that deals with the knowledge of living a healthy life. There are several types of medicaments that are being used in the Ayurvedic mode of treatment. The source of these drugs is diverse and belongs to different category. The category ranges from plants and animals to minerals, and encircles around different types of species of plants and animals with vivid habitats.
In the course of last thirty years, marine organisms have been proven to be a rich source of wide range of worthy compounds for medicine. In Ayurveda there is a wide range of marine drugs like Mukta, Varatika, Praval, Agnijvar, Samudra phena, etc that are useful in the management of numerous diseases like paralysis, hyperacidity, cancer, dyspepsia, eye diseases, etc. This review makes a humble effort to summarize and gather knowledge about different types of marine drugs that are described and explained in Ayurvedic system of medicine, its traditional processing and chemistry, ethno pharmacology and pharmacological role.
Keywords: Hyperacidity, Dyspepsia, Samudra phena, Agnijvar.

INTRODUCTION

Mother nature is one of the greatest giver of miraculous boons to all the living beings of the Earth; probably that's why 80% of the total world population is sill depended over the traditional or natural sources of medicines[1]. Seventy five percent of the Earth is covered by water, hence it is quite obvious that the creatures that dwell in the vast area of marine life, have a great potential to serve the mankind as active medicaments. Marine drugs always remain a focus of interest for emerging scientists and researchers. In the year 2000, the scientists founding the Census of Marine Life converged on a strategy, a worldwide Census to assess and explain the diversity, distribution, and abundance of marine life. The Census encountered an unanticipated riot of species, which are the currency of diversity. It upped the estimate of known marine species from about 230,000 to nearly 250,000. Among the millions of specimens collected in both familiar and seldom-explored waters, the Census found more than 6,000 potentially new species and completed formal descriptions of more than 1,200 of them[2]. Hence it is quite natural that we can discover a vast array of substance of medicinal importance, from the marine source.

Marine drugs in Ayurveda came into existence in different ayurvedic classics in different frame- work of time. The rich periods of Indian system of medicine is broadly divided into five periods,

- Vedic period.
- Ayurvedic period (From pre-Buddhist era to Circa 800 AD)
- The transitional period (From 800 AD to Circa 1100 AD)
- The tantric period (From 1100 AD to Circa 1300 AD)
- The Iatrochemical period (From 1300 AD to Circa 1550 AD)

Marine drugs have made its foot print in almost every period of Ayurveda, starting from Vedic period to the age of alchemy and they come under several categories according to several Ayurvedic classics. Some of them are as following:

- Sadharan rasa group: Group of minerals of least importance for mercurial processing in Indian Iatrochemistry. Agnijvar and Varatika come under this group.
- Kosastha group[3]: Group of animals covered with external shells, like Sambuka.
- Sudha varga: Groups of calcium containing drugs like Sankha, Samudra phena etc.
- Ratna varga: Group of precious gems in Ayurveda. Mukta and praval comes under this group.

Marine drugs in Ayurveda

Sankha

Shankha is the hard calcareous shell of the species of large predatory sea snails, *Turbinella pyrum*, *T. rapa* and *Xanchus pyrum* of Gastropoda, which is the largest class of Molluscus. They are mostly found in shallow ocean coast with abundant sea weed. The most characteristic feature of this class is the spirally coiled shell. According to Rasatarangini it is of two types: Dakshinvarta (rare) and Vamavarta. Vamavarta is very common and hence is therapeutically useful for preparing Ayurvedic medicines[4].

Sambuka

Sambuka referred to all the species that belong to the genum Pila, aquatic gastropod mollusks in the family

Ampullariidae, most commonly known as the apple snails. There are several species of Pila but the most common in India are *Pila globosa , P.olea, P.conica, P. theobaldi, P.virens*, etc. Though Sambuka is mainly found in fresh water, but still the authors of this review had included them because of their close resemblance to Sankha in morphology and therapeutic role[5], the main difference from the Sankha is that the outer covering of Sambuka though hard but still thin as compared to Sankha. The inner fleshy portion is edible and the outer covering is incinerated to get calcium salts.

Samudra-phena

Samudra- phena refers to the Cuttle fish bone. Cuttle fish bone is the internal shell of *Sepia officinalis*, of the family Sepiidae, which is filled with gas and hence aids in buoyancy for the species, they are probably the most intelligent of all invertebrates. The body of the common cuttlefish is flattened and broad, and is therefore oval in cross-section. After the death of the animals the internal shell gets detached and floats over sea water in an isolate manner and get gathered in the sea shore. The description about Samudra-phena in Ayurveda is available from Samhita period[6].

Mukta

Mukta is related to pearl. The knowledge of Mukta is known to India since long time. There are several references of Mukta in Hindu mythology like Sri Madbhagavat, Mahabharata, where they are mostly used as decoration purposes. The internal usage of mukta can be found from Samhita period. According to Ayurveda there are eight sources of origin of Mukta. Among them the Mukta that originate from Sukti (marine shell) is considered to be the best for preparation of medicines. According to the formation, Mukta is of three types. They are natural, cultured and artificial. According to Rasa paddhati, Mukta have three types of lustures. Viz: Madhucchaya-just like honey, Sitachhaya- just like sugar and Srikhandachhaya- just like a preparation made up of curd and sugar[7]. According to Ayurved Prakash, if the Mukta does not loses its shine after rubbing in Sali (a special variety of rice) and washing in cow's urine, then the Mukta is of good quality[8].

Agnijvar

Agnijvar refers to modern day ambergris. Agnijvar is created as a biliary secretion of the intestines of the sperm whale (*Physeter macrocephalus*) and can be found floating upon the sea, or in the sand near the coast. It is found in the abdomen of whales[9] because the beaks of giant squids have been found embedded within lumps of Agnijvar. Scientists have theorized that the substance is produced by the whale's gastrointestinal tract to ease the passage of hard, sharp objects that the whale might have eaten. Agnijvar is usually passed as fecal matter. Agnijvar that forms a mass too large to be passed through the intestines is expelled via the mouth, leading to the reputation of ambergris as primarily coming from whale vomit. Freshly produced Agnijvar has a marine, fecal odor. However, as it ages, it acquires a sweet, earthy scent commonly resembles to the fragrance of rubbing alcohol without the vaporous chemical astringency. Agnijvar is found in lumps of various shapes and sizes, weighing from 15 g to 50 kg or more. Following months to years of photo-degradation and oxidation in the ocean, Agnijvar gradually hardens, developing a dark grey or black color, a crusty and waxy texture, and a peculiar odour that is sweet and earthy. Its odour has been generally described as a vastly richer and smoother version of isopropanol without its stinging harshness. In Ayurveda, Agnijvar is reported for the first time in Iatrochemical period of 12th century classic Rasarnava, written by Bhairavnanda yogi.

Praval

Pravals are marine animals belonging to the class of Anthozoa of the phylum Cnidaria. They typically live in compact colonies of many identical individual "polyps". The red colored coral group includes the important reef builders that inhabit in tropical oceans and secrete calcium carbonate to form a hard skeleton. The internal usage of praval can be seen from Samhita period in Ayurveda. According to Rasatarangini two types of praval are found in use. One is Sakha Praval(contains elongated network of branches of coral and devoid of any pores) and the other type is Moola Praval (containing several pores and round in shape). Regarding the originality of the Praval it is mentioned that if the Praval gets melted just like candle due to application of fire, then we can conclude that the Praval is a fake one[10].

Sukti

Sukti refers to oyster. It is used as a common name for several number of distinct groups of bivalve molluscs of the family Pteriidae, which live in marine or brackish water. The valves of the Sukti are highly calcified. There are two types of Sukti, Mukta Sukti and Jala Sukti. Mukta Sukti are pearl oysters (*Pinctada margaritifera, P. vulgaris, P fucata*) which are generally not eaten by humans. They are harvested for the pearl produced within their mantle and possesses straight long hinge uniting the two valves, the lower valve being a little deeper, than the upper. The surface of the shell is coarse and irregular and ruffled. The internal surface of the valves is of brilliant lusture. Jal Suktis are comparatively small Suktis. Edible Sukti generally comes under Ostreideae. It is divided into three genera. Among these three genera, Crassostrea is common in India. Important species of Crassostrea in India are *C.madrasensis, C. gryphoides, C cucullata* and *C discoidea* [11].

Varatika

Varatika is the external shell of sea animal called *Cypreae moneta* linn. Usually it reaches the coastal areas of the sea and collected by fisherman. The collected animals are dipped in boiled water. The fleshy portion is taken out and used as a diet. At the same time remaining shell is collected and called as Varatika. The upper face is smooth, shining and convex. Base is compressed with a cleft in the center which runs longitudinally. The margin of the cleft is serrated on one side and depressed on the other. Varatika is used to prepare medicines since early days in Ayurveda. According to Rasendrachuramani, Varatika which is yellowish in color, nods at their back

and having a long periphery are considered good. According to the external morphology and heaviness they are of three types. Varatika weighing about 5 gram is considered as best than Varatika weighing 3 gram to 2 gram[12]

Kurmasthi

Kurmasthi is referred to tortoise shell and turtle bone, they are the animals of the order Testudines. They also have medicinal importance according to the Indian system of medicine [13] .

Pharmaceutics

Just like other Ayurvedic Iatrochemical minerals, Ayurvedic marine drugs are at first purified by standard ancient protocol which is known as sodhana and then specific pharmaceutical processing is performed which is known as bhasmikaran (Table 1). In bhasmikaran step the drug is levigated with herbal extracts and dry pellets are prepared. They are enclosed in a close container known as Sarava Samputa and heated in a special arrangement of heat, which is known as Puta, to prepare calcined product known as bhasma of the drug. The calcined product is more therapeutically relevant and biocompatible because particles get converted to nano or sub nano-sized particles[14]. Apart from bhasmas, Praval and Mukta are also pharmaceutically processed by pounding in rose water for specified period until the texture of collyrium is obtained which is known as Pisti. If the pounding is performed under moon light it is known as Chandra puti Praval pisti or Mukta pisti.

Ethnopharmacology of Ayurvedic marine drugs

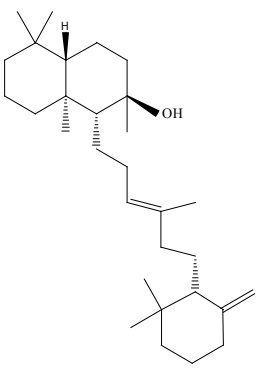
As most of the marine drugs in Ayurveda are rich in calcium salts they are highly effective in combating hyperacidity, dyspepsia and osteoporosis. The calcium salts aids in acid neutralization and bone remineralization. Some are useful in combating mental disorders, paralysis and blood disorders whereas some of them are useful in eye disorders and act as aphrodisiac. (Table 2)

Chemistry of Ayurvedic marine drugs

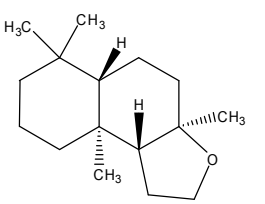
Most of the marine drugs that are mentioned in Ayurveda are rich source of calcium. Sankha, Sukti, Varatika, Sambuka, Mukta, Praval etc are all rich sources of calcium salts.

The fresh shells of Varatika consist of a cellular gelatinous tissue filled with calcareous matter. They contain carbonate of calcium, magnesium phosphate, manganese, fluoride and sodium chloride. In Sukti, Nacre (natural biomaterial with osteogenic properties) is found as the inner shell layer; it is also the outer coating of mukta. It is a strong, resilient, and iridescent in character. Nacre is composed of hexagonal plates of aragonite (a form of calcium carbonate) 10–20 μm wide and 0.5 μm thick arranged in a continuous parallel lamina. These layers are separated by sheets of organic matrix composed of elastic biopolymers (such as chitin, lustrin and silk-like proteins). The mineral of nacre is calcium carbonate which is highly crystallized as aragonite. The FT-IR spectra showed amide, amine, and carboxylic acid groups in the organic matrix of the whole (organic and mineral) nacreous layer, with the HCO_3 groups possibly at the organic-mineral interface. The insoluble organic matrix remaining after decalcification contain amide, amine, and carboxylic groups. On heating during bhasmikarana process in Mukta, aragonite mineral structure of nacre underwent two transformations, aragonite to calcite at 300–400°C, and calcite to calcium oxide at 500–600°C. The organic matrix of nacre gets destroyed at 550–600°C. Calmodulin-like protein is also believed to be involved in the shell formation of Mukta sukti. In Sukti, Conchiolin and perlucin are complex proteins which are secreted by a Sukti's outer epithelium to form chambers. These chambers hold and bound to the crystals of aragonite, giving the Sukti's shell its stiffness[29].

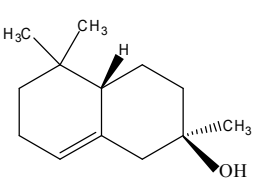
The first chemical investigation of the constituents of Agnijvar was carried out in Paris in 1820 by Pelletier and Caventon, who found that its major component is tricylic triterpene. Study revealed by chromatographic methods, confirm the presence of ambrein (triterpenoid) as well as some other sterols. The saponified portion was reported to contain stearic, oleic, linoleic, archidic and betenic acids. The odour of ambergris is due to the presence of oxidation products of ambrein. Agnijvar contains ambrein as the major constituent, which can be separated from ambergris by heating in alcohol. Ambrein**(I)** get oxidized to ambroxan**(II)** and ambrinol**(III)**, which are the most important odour producing chemicals in ambergris[30].



(I)Ambrein



(II)Ambroxan



(III)Ambrinol

Pharmacology of Ayurvedic marine drugs

Anti ulcer activity

- Study revealed that Shankha bhasma rendered dose dependent protection against experimental gastric ulcers induced in rats by indomethacin and cold restraint stress model. Shankha bhasma caused significant reduction in ulcer index in both the indomethacin and cold restraint models. Thiobarbituric acid reacting substances of stomach in indomethacin treated rat was also reduced by Shankha bhasma but serum calcium level was not altered[31].
- Study revealed that Mukta bhasma produced significant protection in cold restraint stress induced gastric ulcer and diclofenac induced ulcer in low doses of therapeutic range when compared with control. Thiobarbituric acid reacting substances of stomach in ulcer induced rat was also reduced by Mukta bhasma[32]
- Study revealed that Muktashukti bhasma possess variable reduction in free and total acidity, peptic activity and acid output in pyloric ligated rat model[33].

Table 1: Traditional pharmaceutical processing of marine drugs in Ayurveda

Ayurvedic marine drugs	Purification	Pharmaceutical processing
Sambhuka[15]	Sambhuka is purified by boiling in lemon juice for one and a half hour.	It is levigated with *Aloe vera* juice and pellets are prepared. These pellets are heated up to 1000^0C, in enclosed container to obtain white coloured bhasma
Samudra phena[16]	It is purified for internal use by scrapping the outer surface and triturating with lemon juice and then dried.	Bhasma is not prepared.
Mukta[17]	Purified by boiling with the leaves of *Sesbania aegyptiaca* for three hours.	It is levigated with cow's milk and heated up to 800^0C, in enclosed container to obtain white coloured bhasma
Agnijvar[18]	Due to alkaline nature of the sea water, Agnijvar already gets purified.	Bhasma is not prepared.
Praval[19]	Purified by boiling with the juice of leaves of *Sesbania aegyptiaca* for three hours.	Levigated with *Aloe vera* juice and then heated in enclosed container. The process is repeated for three times.
Sankha[20]	Sankha is purified by boiling in lemon juice for twelve hours.	It is broken into small pieces and kept in enclosed container. This container is heated up to 1000^0C, to obtain white coloured bhasma. The process is repeated for another time.
Sukti[21]	Purified by subjecting it to boiling with the juice of *Sesbania aegyptiaca* or any acidic substance.	It is powdered and pellets are prepared by subjecting it to levigation with *Aloe vera* juice. Then it is heated to 1000^0C in a closed container. The process is repeated 2 times, to obtain a fine bhasma.
Varatika[22, 23]	Purified by boiling in acidic medium for 3 hours.	Purified Varatika is taken in enclosed container and heated to 1000^0C to obtain fine white bhasma.
Kurmasthi[13]	Kept in water filled container for 12 hours and then dried.	It is levigated with *Aloe vera* juice and pellets are prepared. These pellets are heated up to 1000 ^{0}C, in enclosed container to obtain bhasma.

Table 2: Ethno pharmacology of Ayurvedic marine drugs

Ayurvedic marine drugs	Traditional use	Formulations
Sambhuka	Sambhuka bhasma is useful in abdominal colic, hyperacidity, eye disorder and diarrhea. Internal flesh is use as oil in otitis media and painful discharge from the ears[24].	Sambhuka taila[24], Sambhuka bhasma, etc.
Samudra phena	Useful in eye diseases(for removing scars)[25], skin diseases and painful exudation from ears.	Sukha vati varti, Dristi pradan varti, Samudra fena varti[25], Danta varti, etc.
Mukta	Useful in fever, diabetes, cough and cold, eyedisorder, osteomalacia, osteoporosis, burning sensation, dyspepsia. It is a good tonic for mental ability[26].	Muktadi churna, Hema garvha pottali rasa, Kumudeshwar ras, Indrokta rasayan, etc.
Agnijvar	Useful in paralysis, hemiplagia, paraplegia, blood disorders and cancer. It is a good remedy for tetanus. It is also useful for controlling obesity and is an excellent aphrodisiac[18].	Jawarmohora vati, Dhatri rasayan, Chintamani ras, etc.
Praval	Praval pisti and praval bhasma are useful in eye disorders, hyperhidrosis, burning sensation in the body. It is useful to enhance the complexion of the face, haemophilia, tonsillitis, general dibility and benign prostatic hypertrophy[27].	Kasturi vairav ras, Kandarpa sundar ras, Vasantamalati ras, Praval panchamrita, etc.
Sankha	Useful in hyperacidity, dyspepsia, gastroesophageal reflux. It is very useful for eye diseases and is used as collyrium[25, 28]	Kaphketu ras, Sankha drava, Sankha bhasma, Praval panchamrita ras, etc
Sukti	Useful in glycosuria, abdominal tumor, spleen disorder and abdominal colic. Act as an antidote, digestive and carminative [11].	Grahani sardula rasa, Praval panchamrita ras, Astamrta bhasma, Mukta panchamrita ras, etc.
Varatika	Useful in dyspepsia, eye disorders, aphrodisiac and act as general antidote[12]	Raj mriganka ras, Praval panchamrita ras, Pradarantak lauha, Agnikumar ras, etc.
Kurmasthi	Useful in osteoporosis, act as tonic in general debility. It is very useful in epilepsy[13]	Kurmasthi bhasma

Anti Osteo arthritis effect

Study revealed that Praval bhasma is effective in the prevention of calcium and estrogen deficient bone loss which was induced by ovariectomized and concurrent calcium deficient female rat model and thus the use of Praval bhasma in traditional system of Indian medicine for management of bone metabolic disorders such as osteoporosis, osteoarthritis and osteomalacia is justified by the research study[34].

Cytotoxic activity

Study revealed that ten new derivatives of ambrein, isolated from Agnijvar, which was prepared by chemical transformation, exhibit cytotoxic activities against human liver carcinoma, colon adenocarcinoma, lung carcinoma and human breast adenocarcinoma cell lines. The anti-inflammatory activities in terms of the inhibition of human neutrophil function were also evaluated for ambrein[35].

Hormonal activity

Study revealed the positive effects of Agnijvar in both sexual desire and body weights due to its effect on some endocrine hormones. There was significant increase in testosterone, estradiol, prolactin, insulin, cortisol, thyroxin (T4) levels and body weights after Agnijvar administration. A significant increase in total cholesterol, low density lipoprotein cholesterol and high density lipoprotein cholesterol was investigated while significant decrease in triglycerides levels in Agnijvar treated group were also observed[36].

Anti cataract activity

Study revealed that Ayurvedic eye drops containing Mukta has significant anti cataract activity. Anti-cataract potential was evaluated using steroid induced cataract in developing chick embryos, sodium selenite induced cataract in rat pups and galactose induced cataract in rats. Result revealed significant anti-cataract activity by inducing noticeable delay in the progression of cataract in the selenite and galactose induced cataract models[37].

Aphrodisiac activity

Research revealed that ambrein, a major constituent of Agnijvar, have positive activity on masculine sexual power on rats. Male sexual activities were assessed by recording the penile erectile responses and homosexual mountings in the absence of female. The copulatory studies were carried out by caging males with receptive females. After recording the copulatory pattern of treated male rats, ambrein produced recurrent episodes of penile erection, a dose-dependent, vigorous and repetitive increase in intromissions and an increased anogenital investigatory behavior[38].

Anti diabetic activity

Study revealed that ambrein from Agnijvar reduced the blood glucose level of normal and moderately alloxan treated diabetic rats by enhancing glucose utilization. Ambrein did not reduce the hyperglycemia of glucose-loaded rats in the presence of mannoheptulose but it reduced the hyperglycemia of glucose-loaded rats in the absence of mannoheptulose[39].

CONCLUSION

Thus we see Ayurveda; the traditional Indian system of medicine has a rich history of utilization of marine drugs. There is a complex pharmaceutical processing of these drugs which convert them to more biocompatible *bhasma* (calx) form, and hence causes direct enhancement in their bioavailability. The main chemical constituents of these drugs are calcium carbonate, but they also contain trace amount of other minerals, which results in the difference of therapeutic efficacy. The ethno pharmacological and traditional role of these marine drugs in the treatment of hyperacidity, gastric reflux disease, dyspepsia, sexual incompetency, etc is supported by modern pharmacological findings. Further research work and theoretical work in this field is welcomed, from budding researchers.

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