SIDDHA LITERATURE EVIDENCES ON MARINE SOURCES FOR THE MANAGEMENT OF ACQUIRED IMMUNODEFICIENCY SYNDROME

Jothi J[1*], Balagurusamy K[2], Suresh S[3], Jeeva Gladys R[4]

Article History: Received: 10.03.2023 **Revised:** 31.05.2023 **Accepted:** 10.07.2023

[1*]Associate professor, National institute of Siddha, Tambaram sanatorium, Chennai- 600047.
[2]Principal, Velumailu Siddha Medical College, Sriperumbudur, Kancheepuram, Tamil Nadu – 602105.
[3]Professor, Velumailu Siddha Medical College, Sriperumbudur,Kancheepuram, Tamil Nadu - 602105
[4]Associate professor, Department of sool & magalir maruthuvam, Velumailu Siddha Medical College, Sriperumbudur,Kancheepuram, Tamil Nadu - 602105

[*]Corresponding Author
Dr. J. Jothi[1*]
[1*]Associate professor, National institute of Siddha, Tambaram sanatorium, Chennai- 600047.
Email: jo.athma@gmail.com

DOI: 10.31838/ecb/2023.12.6.244

1. INTRODUCTION

Marine environment is the richest and most complex ecosystem containing substances with excellent biological activities. Products derived from marine organisms have been recommended in alternative system of medicine such as Coral, pearl, oyster shell, conch are the marine based raw drugs widely used in Siddha system of medicine for several treatments. Approximately 7000 marine natural products have been reported, among these 33% from sponges, 18% from coelentrates (sea whips, sea fans and soft corals) and 24% from representatives of other invertebrate phyla such as ascidians (also called tunicates), opisthobranch molluscs (nudibranchs, sea hares, etc.), echinoderms (starfish, sea cucumbers, etc.) and bryozoans. Among invertebrates, molluscs are widely distributed throughout the world and have many classes of bioactive compounds exhibiting anti-tumor, anti-leukemic, antibacterial and antiviral activities have been reported worldwide. [1]

Definitions of 'marine biotechnology' often refer to the vast potential of the oceans to lead to new cures for human and animal disease. Natural drug discovery from the world's oceans has been accelerated by the chemical uniqueness of marine organisms and by the need to develop drugs for contemporary, difficult to cure, diseases. Current research activities have generated convincing evidence that marine drug discovery has an exceedingly bright future. [2]

Marine microorganisms are found in symbiosis with marine sponges, corals and other species. Hence, they are a natural marine enzymes and various bioactive peptides which are antimicrobial compound and has served as a natural source of drug discovery since ancient times. . Various compounds that may prove to be therapeutically effective still remain unexplored scientifically. [3] Nearly half of the worldwide biodiversity is constituted by different types of marine species and as a result, oceans, sea are enriched with valuable natural bioactive compounds such as proteins, peptides, amino acids, fatty acids, sterols, oligosaccharides, vitamins, and minerals, etc. These agents also help to enhance the nutritional as well as the therapeutic value of the Sea products. Every year nearly thousands of new compounds are isolated from marine organisms which further help in the discovery of new leads for the development of new drugs to treat or diagnose human diseases like cancer, viral diseases, inflammation, etc. [4]

Overview of selected marine products in Siddha literature

Research on marine organisms began in the last century but a number of marine products are in use in Siddha system of medicine since time immortal. Pearl, coral, oyster shell, marine shell, conch shell, *amber* are some examples used as medicine in this system.Pavalam (Corallium rubrum) of marine origin belongs to the phylum Cnidaria. It has a fragmented pattern of distribution and occurs in the western Mediterranean, in some parts of the eastern Mediterranean and in the neighboring Atlantic coasts such as those of Morocco. [5] It is available in Maldives, Lakshadweep and Rameshwaram in India. [6]

Pavalam-Red coral is made primarily of Calcium carbonate in the form of calcite including 5% of other elements such as Mg, Fe, So4, P2O5, Sio2, Pb,Zn and an organic matrix. [7] Pearls are calcareous concretions which are formed as protection against the minute particles or parasites which penetrate between the mantle and shell causing irritation in the mollusc. Consequently, these foreign objects deposit and form as an irregular or spherical shaped blister under the layer of the shell obtaining Pearl. Very frequent usage of pearl powder is at the highest rank in the pharmaceutical and cosmetic industry. Pearl is used in ash form for its potential as an oral immunomodulator. Therefore, pearl used in ash, calcinated and powder form isused to treat various illnesses which include heart weakness, myocardial degenerations, tuberculosis and habitual abortions. [8]

Pinctada margaritifera is the zoological name of black lipped Indian pearl oyster. The natural sources of pearl oyster are sea beds. The species Pinctada Margaritifera are widely distributed throughout the indo-pacific region.

They are invertebrates and have axo-skeleton in the form of shell. The shell of the pearl oyster is reddish brown in colour. The nacreous portion of the shell has bright metallic luster. The non-nacreous border as brownish or reddish patches corresponding to the external radial markings. The crystals of calcium carbonate and magnesium carbonate present in the shell is responsible for the medicinal property of these shells. [9]

Muthu chippi(Pearl oyster shell), one among the Siddha drugs derived from the sea contains Calcium Carbonate, phosphate and sulphate of calcium and magnesium, Iron oxide, alumina and Silica. [10] Pearls have the same physical properties and composition of natural shell nacre, with calcium carbonate as the main component and pearl formation had thus been termed bio-mineralization [11]

Palagarai-Shell of Cypraea moneta is found to be effective in anti-pyretic, antiinflammatory, anti-microbial activity and the presence of cardenolides contributes to the role Cardiac activity and Analgesic activity. Powdered Pearls from shells has some anti-inflammatory effect on conjunctivitis where the surface of the eye becomes red and sore. [12]

Ambra Grisea, it is a faecal product of the sperm whale (Physeter catodon), which has long been prized in eastern practice as medicine, condiment or perfume. [13] It shows the effects of curing migraine headaches, common colds, constipation and improving sexual performance.[14]

The main three components isolated from *Ambra grisea* (ambergris) are: triterpene alcohol ambrein, epicoprostanol and coprostanone, the first being the principal active ingredient. Breakdown of the relatively scentless ambrein through oxidation produces ambroxan and ambrinol, the main odor components of ambergris. Ambergris has been mostly known for its use in creating perfume and fragrance much like musk. This substance has also been used historically as a flavoring for food and is considered an aphrodisiac in some cultures.[15]

Biomedical value of molluscs lies in their secretions, which originate from the dermal region or from internal glands. Molluscan shell is one of the important raw materials for calcium and calcium based industries. It contains 33 to 40% of calcium, of which 90 t0 98% occur as calcium carbonate. Among the five basic natural elements, conch shell has predominant composition of water. [16] Siddha literature evidences on Marine resources with scientific relevance [17]

S.No	**Marine Product**	**Therapeutic actions based on Siddha text**	**Anti-HIV property**	**Reference Use name et al., year**
1.	*Muthu* (Pearl)	Aphrodisiac, Expectorant, Nutrient, Haemostatic, Anti-dote,Antimicrobial, Anti-spasmodic	Present Inhibit HIV-1 protease	[17][18]
2.	*Muthu Chippi* (Pearl oyster)	Nutrient, Demulcent, Stomachic, Cardiaoprotective	Present Inhibit HIV-1 protease	[19][20]
3.	*Pavalam* (Coral)	Nervine tonic, Diuretic, Purgative, Astringent	Present Cnidarins as a novel class of highly potent proteins in coral reef capable of blocking the HIV virus from penetrating T-cells.	[21][22]
4.	*Palagarai*	Expectorant, Sedative,	Present	[23][24]

	(Marine shell)	Febrifuge, Rubefacient Useful in Tuberculosis,Chronic diarrhoea,malarial fever,eye-disease, Jaundice,Hepatomagaly, spleenomegaly	The sulfated chitin and chitosan have anti-HIV property	
5.	*Amber* (*Ambra grisea*)	Stimulant, Aphrodisiac, Nutrient, Anti-spasmodic.Useful in epilepsy,sloughing ulcers.	Not reported	
6.	*Sangu* (Conch shell)	Nutrient, Anodyne, Carmenative, Stomachic, Astringent, Expectorant	The sulfated chitin and chitosan have anti-HIV property	[25][24]

Human Immunodeficiency Syndrome (HIV)

Patients infected with the human immunodeficiency virus (HIV) display a broad spectrum of clinical manifestations, ranging from no symptoms to life threatening illnesses caused by a wide range of pathological processes. Previously healthy individuals developed a range of infections normally seen when cellular immunity is impaired. This syndrome became known as the acquired immunodeficiency syndrome (AIDS). About 2 weeks after infection with HIV approximately 50% of patients will develop a viral illness which may resemble glandular fever, influenza or aseptic meningitis. In more severe cases, hepatomegaly and raised transaminases may be detected. The number of CD4 lymphocytes falls transiently and may be associated with opportunistic infections.

Following recovery from the acute infection there is a prolonged latent period, often lasting several years. There is little evidence of viral activity in the peripheral blood with normal CD4 lymphocyte counts and only a few HIV-infected cells. There is often a generalized lymphadenopathy, however, and examination of lymphoid tissue reveals active and progressive disease. As the disease progresses there is a fall in the number of CD4 lymphocytes while the proportion that are HIV-infected rises. Clinically, this is associated with a succession of opportunistic infections, reactivation of dormant infections and an increased incidence of Kaposi's sarcoma and lymphomas. The mean period between infection and the development of AIDS is 10 years.[26]

Effectiveness of Marine resources in pathophysiology of AIDS

Immunodeficiency and microbial infections

HIV disease progression and transmission are strongly associated with blood viral burden. An increased concentration of human immunodeficiency virus type-1 (HIV-1) has been observed in the blood independent of CD4+ cell count. High concentrations of HIV-1 RNA in the blood are predictive of disease progression, and correlate with the risk of blood-borne, vertical, and sexual transmission of the virus.[27] Microbial translocation and innate immune action characterize HIV infection. Increased immune activation has been linked to microbial translocation during both untreated and treated HIV infection. compromised barrier function and translocation of microbial products from the gut lumen into the systemic circulation have been implicated as one potential cause of persistent immune activation during chronic HIV infection. Microbial products can cause systemic immune activation via activation of innate sensors including Toll-like receptors, activating myeloid lineage cells, and inducing immunoregulatory enzymes like IDO.[28] HIV-1 infected individuals had lower Relative abundance of *Faecalibacterium*, *Coprococcus* and *Roseburi*

a genera which are known to contain several butyrate-producing bacterial species. Loss of colonic mucosal BPB, with a presumptive decrease in mucosal butyrate levels, in conjunction with increased abundance of pro-inflammatory, pathobiont commensal bacteria could promote unregulated inflammatory responses and mucosal HIV-1 replication. [29]

Pavala parpam a Siddha formulation is prepared from coral reefs and calcinated (Parpam) using herbal decoctions and incineration (Pudam) for the management of respiratory symptoms such as cough, copious phlegm, fever, and breathing difficulty. Research studies report that Pavala parpam was found to be effective against microbial type culture collection strains of Neisseria mucosa, Klebsiella pneumonia, Streptococcus pneumonia, Staphylococcus aureus, Pseudomonas aeruginosa, and Aspergillus niger, respectively.[30]

The constitutents of muttuchippi are Calcium carbonate 85 - 95%, Phosphate and Sulphate of Calcium and Magnesium. [31][32] Magnesium regulates anti-viral immunity. [33] Mn2+ is released from organelles and accumulates in the cytosol upon virus infection, activates anti-viral innate immunity via the cGAS-STING pathway and increases the sensitivity of cGAS to dsDNA and promotes STING activation. [34] Vitamin D deficiency is highly prevalent among HIV patients and is a potential modifiable factor (combined with calcium supplementation) for improving musculoskeletal health. [35] [36]

The anti microbial study reveals that Pavala Parpam has significant anti bacterial activity. The tested strains such as Streptococcus mutans, P.aeruginosa, E.Coli, Staph aureus,K.Pneumonia were found to be highly sensitive to Pavala Parpam.

Nervine Tonic

Neurotoxic factors in HIV have been incriminated, which may act in combination: viral proteins, particularly *gp120, gp41, tat, nef*, or substances produced by activated glial and microglial cells such as cytokines, prostaglandins, proteases, arachidonic acid or quinolinic acid metabolites. Viral proteins, such as tat, can also be transported along neural pathways, they can cause neurotoxic damage at remote sites. A glutamate-mediated excitotoxicity increased glutamate levels in the cerebrospinal fluid (CSF) and plasma of patients with HIV-related dementia. Increased levels of quinolinic acid, a glutamate agonist, are present in the CSF of AIDS patients with cognitive and motor abnormalities. In addition, in HIV infection, activated microglial cells may express the high affinity glutamate transporter "excito amino acid transporter-1", while its normal expression by astrocytes is inhibited . Although each of these toxins can damage nerve cells, it has been shown that a combination of cellular and viral factors induces a more severe degree of neuronal apoptosis that each of them in isolation. This has led to the suggestion that neuronal apoptosis and consequent neuronal loss in HIV-infected patients may be multifactorial . The mechanism of the final irreversible stage of neuronal DNA damage and eventual apoptosis appears to involve oxidative stress and glutamate-receptor-mediated toxicity.Combined HIV protein and cytokine neurotoxicity may be mediated by oxidative stress and cause neuronal apoptosis. Neurotoxic HIV proteins can initiate a cascade of events that self-perpetuate in a positive feedback manner for nerve cell damage.[37] Manifestation of central nervous system changes includes seizures, hemiparesis, aphasia or changes in cognitive functioning, including personality changes, inability to concentrate, memory impairment, generalized confusion and obtundation that can progress to coma. [38]

Psychiatric symptoms among patients with acquired immune deficiency syndrome (AIDS) may be functional reactions to contracting a fatal and stigmatizing disease or may be secondary to malignancies and opportunistic infections in the central nervous system (CNS). Recent evidence indicates that HTLV-III, the virus that causes AIDS, directly infects the CNS and may cause psychiatric symptoms before signs of immunodeficiency, cognitive impairment, or neurological abnormalities emerge. AIDS-related organic mental syndromes may mimic functional

disorders such as chronic mild depression and acute psychosis.[39]

Up to 70% of patients who have AIDS develop neuropsychiatric symptoms due to toxoplasmosis encephalopathy, cryptococcal meningitis, progressive multifocal leukoencephalopathy, neurologic HIV infection, metabolic derangements, fever, hypoxia, and other causes. Symptoms range from poor concentration, forgetfulness, and altered mental status to severe dementia or delirium. Psychiatric symptoms including depression, anxiety, and agitation are also common. [40] HIV does not directly injure neurons by productive infection but via infection of macrophages and microglia and the by-products of inflammation. This indirect mechanism leads to damage of selected neuronal populations and white matter tracts and, in many cases, precedes severe and rapidly progressive cognitive impairment.[41]

AIDS is a great mimicker which can present in almost any neurological manifestation. Epilepsy is not an uncommon neurological manifestation associated with AIDS. Encephalitis was found to be the commonest cause of epilepsy followed by meningitis, brain abscess, CNS lymphoma and toxoplasmosis. Out of the 700 Sudanese AIDS patients almost 5.71% had epilepsy and 50% of them had generalized convulsions.[42] The preliminary biochemical study of Pavala Parpam reveals the content of calcium, ferrous, chloride, carbonate, tannin, tannic acid, unsaturated compounds and alkaloids. Since the presence of calcium (37.48%), ferrous, tannin, and tannic acid, it has the action of haemostatic. Calcium – Plays the important role in the coagulation of blood. It is the IV factor in coagulation mechanism. It acts by converting prothrombin to thrombin and also necessary for the formation of both intrinsic and extrinsic thromboplastin. It is required for the maintenance of the capillary permeability. [43]

Findings of a research study reveal, the test drug Muthu Parpam was effective in inhibiting the AChE enzyme at the specified concentration in a dose-dependent manner. Maximum percentage inhibition of about 71.68% was observed at 500µg/ml when compared to that of the Physostigmine, a known AChE inhibitor with a maximum inhibition of 84.87% at the concentration of 40µg/ml.As a result, this preliminary screening has demonstrated the neuroprotective activity of Muthu parpam in the management of Alzheimer disease via AChE inhibition potential.[44]

Oral Candidiasis and Opportunistic infections

HIV infected individuals begin to develop manifest clinical expressions linked to HIV, such as oral/candidiasis (thrush), oral hairy leukoplakia and constitutional symptoms such as sustained weight loss, fever, fatigue, night sweats and persistent diarrhea. AIDS is characterized by a number of opportunistic infections, neoplasms and HIV wasting syndrome and AIDS-related conditions and can affect virtually every organ/system of the body. Gastrointestinal manifestations are particularly common and cause dysphagia, postprandial emesis, hematemesis, diarrhea, abdominal pain, malabsorption, malnutrition and weight loss.[38]

According to previous research reports, Oyster shell and heat-treated oyster shell were made of $CaCO_3$ and CaO, and had a lot calcium ions. They may first be attracted to fungi surfaces by electrostatic bonding between calcium cationic and anionic structures on the fungi surface. When the membrane was destabilized by calcium cation via ion exchange and formation of transmembrane pores, disturbing and lysis of fungi cells occurred.[45] Hence Muthu (Pearl) and Muthu chippi (Oyster shell) may have antifungal effects in this mechanism.

Ocular manifestations

The ocular complications of human immunodeficiency virus (HIV) infection have been widely documented and Cytomegalovirus (CMV) retinitis is a leading cause of blindness among HIV infected patients. Herpes zoster ophthalmicus is uncommon and usually occurs in earlier stages of HIV disease. Kaposi's sarcoma, anterior uveitis and conjunctival squamous cell carcinoma has been found in HIV infected patients. The most frequent eye problem was HIV related microvasculopathy, which was present in

10% of the patients. Its frequency increases with the stage of HIV disease. [46]

Ocular syphilis is found in less than 1% of persons with HIV infection and it tends to have more aggressive, severe, and relapsing manifestations than in immunocompetent persons. Findings include granulomatous or nongranulomatous anterior uveitis, panuveitis, necrotizing retinitis, optic neuritis, papillitis, chorioretinitis, vitreitis, retinal detachment, branch retinal vein occlusion, interstitial keratitis, and scleritis. Blindness may occur.[47]

Ocular changes in the HIV-infected individual, most often associated with opportunistic infections (especially cytomegalovirus), may be accompanied by severe visual impairment and in some cases blindness. Ocular disease associated with HIV infection is common and reduces quality of life, but is typically not life-threatening. Findings may include a noninfectious microangiopathy, consisting of cotton-wool spots with or without retinal hemorrhages. This retinopathy occurs in two thirds of AIDS cases but can also appear less frequently with HIV infection. The HIV envelope glycoprotein may induce an inflammatory state in retinal pigment epithelial cells, impairing its integrity and contributing to retinopathy.

In Anuboga Vaidhya navaneetham, attributes the Pavala Parpam as Sanjeevi drug particularly in the management of bleeding from the organs. Pavalam (Coral) is used to treat Kaba diseases, Osteoporosis, Bleeding disorders, Cough, Insect bite, Spermatorrhoea, Bronchial asthma and Diabetes. It is classified under the topic Uparasam by sage Bogar. [6] All the Pavalam included formulations are found to possess diuretic, laxative, astringent, nervine tonic and spermatogenesis properties and useful in the treatment of Azhal aggravated diseases, excessive phlegm and eye disorders.[48] Sangu (Conch shell is being used in various eye formulations such as Kankaasa mathirai, manosilai mathirai, santhirodhaya mathirai,Macha rathinaathi mathirai.[49]
Opportunistic ocular infections are frequent with cytomegalovirus (CMV) and infrequent with Toxoplasma gondii, Pneumocystis jiroveci (carinii), herpesviruses, Cryptococcus, Candida, Histoplasma, and atypical mycobacteria. Kaposi sarcoma and malignant lymphomas may infrequently involve conjunctiva, eyelid, or orbital tissue. Neuro-ophthalmic lesions (cranial nerve palsies, optic neuropathy, papilledema) appear in less than 10% of AIDS cases but frequently accompany cryptococcal meningitis.[47]

Antitubercular actions

Mycobacterium tuberculosis (MTB) is being seen with increasing frequency as a complication of HIV infection. By computed tomographic (CT) scan, mesenteric lymphadenopathy with low attenuation suggestive of necrosis, and occasional soft tissue attenuation, can be due to MTB. Tuberculous peritonitis on CT scan reveals high-attenuation ascites along with peritoneal and omental nodules.[48] The sites for involvement with tuberculous lymphadenitis include cervical lymph nodes in virtually all cases, followed by axillary involvement in 82%, ilioinguinal in 54%, and epitrochlear in 36%. The nodal size ranges from 1 to 3 cm, and involvement is usually symmetrical. The presentation overlaps with HIV lymphadenopathy.[906] Histologically, with MTB infection there is usually a recognizable localized granulomatous reaction, including caseous necrosis. Langhans giant cells, lymphocytes, epithelioid macrophages, and fibrosis are present in variable numbers. Acid-fast tissue stain reveals rod-shaped acid-fast microorganisms similar to that described in non-HIV-infected patients. The organisms in the lesions are never as numerous with M tuberculosis as with MAC.[47]

Chronic diarrhoea

HIV has been demonstrated to infect gastric epithelial cells. The most frequent clinical symptom resulting from GI involvement is diarrhea, and the etiologies for this symptom are numerous. Diarrhea may appear with acute HIV infection, but typically it is manifested in patients with clinical AIDS. In a few cases this diarrhea may be severe and life threatening. In patients receiving antiretroviral therapy (ART), the frequency of gastrointestinal involvement with

opportunistic infections is greatly diminished. When the CD4 lymphocyte count is below 200/μL, the likelihood of finding an infection in association with diarrheal illness is increased.[47]

Malarial fever

HIV infection increases the risk of an increase in the severity of malaria infection and burdens of malaria, which in turn facilitates the rate of malaria transmission. Malaria infection is also associated with strong CD4+ cell activation and up-regulation of proinflammatory cytokines and it provides an ideal microenvironment for the spread of the virus among the CD4+ cells and for rapid HIV-1 replication. Marine-derived bioactive peptides have been isolated widely by enzymatic hydrolysis of marine organisms [50] [51] They observed and isolated two peptides, Leu-Leu-Glu-Tyr-Ser-Ile (1) and Leu-Leu-Glu-Tyr-Ser-Leu (2), which inhibited HIV-1 protease in thermolysin hydrolysate of oyster protein. The peptide 1 and 2 showed strong inhibition of HIV-1 protease at IC50 values of 20 and 15 nM, respectively. Moreover, these peptides behaved as competitive inhibitors for HIV-1 protease with *K*i values of 13 and 10 nM, respectively. Lee and Maruyama confirmed that the presence of C-, N-terminal hydrophobic amino acids and the length of the amino acid sequence in these peptides are important for their inhibitory activity.[20]

More effective sexual transmission of HIV and an accelerated progression to clinical disease is seen in people with elevated concentrations of HIV-1 RNA in the blood. *P. falciparum* infection promotes macrophages and CD4+ cells to activate viral transcription and elicits a strong immune response, leading to a high turnover of HIV-1 RNA and fever indicates a cytokine response that might raise HIV-1 RNA concentrations. [27]

Hepato/spleenomegaly

Abnormalities in liver-associated enzymes are commonly present in HIV-infected patients, and liver histology is almost always abnormal. Although abnormalities in liver-associated enzymes are present in most HIV-infected patients, jaundice is rather infrequent. Potential causes of jaundice are drug-induced hepatitis (31%), alcoholic liver disease (13%), and opportunistic infections or neoplasm (30%). Jaundice, when present, was associated with a high mortality which may be due to a difference in the incidence of intravenous drug abuse, sexual practices or yet unidentified causes.[52]

Hepatomegaly and abnormalities of serum liver tests are common problems in patients with acquired immune deficiency syndrome. Opportunist infections *(Mycobacterium avium-intracellulare* and cytomegalovirus) and neoplasms (lymphoma, Kaposi's sarcoma) are among the most prevalent hepatic lesions in AIDS. Drug hepatotoxicity, multimicrobial infections of the biliary tree resembling sclerosing cholangitis and a variety of nonspecific hepatic changes should be considered in evaluating AIDS patients or HIV-1-infected patients with evidence of liver dysfunction.[53] Splenomegaly is a common clinical finding in patients with AIDS, and it is present at autopsy in about one third of AIDS cases. Opportunistic infections or neoplasms are more likely to be present when the splenic weight is greater than 400 g. Weights of up to 1 kg can occur.[911] The most frequent splenic findings at autopsy are M avium complex (MAC), M tuberculosis (MTB), cryptococcosis, cytomegalovirus, Kaposi sarcoma, and malignant lymphomas (Table 5). Gross pathologic lesions consist of a prominent follicular pattern in about half of AIDS cases and a miliary granulomatous pattern in about 10%.[911] Sepsis may lead to a soft, almost liquid splenic parenchyma. Splenic infarcts may occur with embolization from non-bacterial thrombotic endocarditis or infectious endocarditis involving mitral or aortic valves.[47]

Pharmacological analysis shows that the test drug Pavalaveerachunnam which has pavalam (Coral) as its ingredient has got good significant. Hepatoprotective, Hypolipidemic, Diuretic activity when compared to the standard drug.[54]

Mucosal sloughing and ulceration

Anal and/or rectal localization of tuberculosis, even in immune-compromised patients is rare. Tuberculous enteritis bacili penetrate the mucosa

and infect the submucosal lymphoid tissue, resulting in the epitheloid tubercle with Mucosal sloughing and ulceration. [55]

Candida esophagitis, a superficial mucosal infection, is one of the most common opportunistic infections in patients with acquired immunodeficiency syndrome (AIDS) resulting in ulceration, extent of candidiasis, and showing of viral cytopathic effect.[56] Generally, Pavalam has Thuvarppu suvai (Astringent) which has the property of arresting the bleeding arising from the organs.Recently, organic materials extracted from the corals are used in the studies of anti-HIV drug.Pavala Parpam exhibits significant reduction in both bleeding and clotting time when compared to untreated control animal's blood. The significant reduction in bleeding with Pavala Parpam is well comparable to that of Adrenochrome, a standard haemostatic drug.[57]

Aphrodisiac

AIDS remains a problem mainly for individuals engaging in identifiable and preventable high-risk behaviors which, over time, deplete and destroy the immune system. These factors include: promiscuous and unsanitary anal intercourse, trauma, anonymous-sex lifestyle, associated or independent chronic use of aphrodisiac sexual stimulants, psychoactive drugs, amphetamines, alcohol, antibiotics, other immune-system depleting substances and malnutrition.[58]

In HIV infection, infertile patients with Testicular microlithiasis had primary testicular failure. Some have suggested that the microlithiasis cause infertility.[59] Ambrein, a major constituent of ambergris has supportive activity on masculine sexual ability on rats. The copulatory studies were conducted by caging males with receptive females. After observation the copulatory behavior of treated male rats, ambrein formed repeated incidents of penile erection, a dosedependent, strong and repetitive rise in intromissions and an amplified anogenital investigatory performance [60] This study has been proven to increase sexual behavior in rats, which providing some support for its traditional aphrodisiac use

Gastrointestinal manifestations

The gastrointestinal tract is one of the most involved organs by HIV/AIDS, with lesions in the mesentery, peritoneum and retroperitoneum. HIV/AIDS related gastrointestinal diseases can be divided into two types, including inflammations and neoplasms, such as CMV infection and KS. These diseases can involve all kinds of tissues in the digestive system. For instances, Candida mainly invades oral cavity and esophagus, while protozoa infection often involves colon to cause chronic diarrhea. KS commonly occurs in esophagus, followed by the small intestine and colon in frequency of occurrence. Lymphomas mostly occur in small intestine and colon.[61] Among the marine species, Sangu (Conch shell, Chank) plays a very important in the preparationof *Sangu Parpam*, a medicine very frequently prescribed by all the Indian Medicine Doctors for Peptic Ulcer (Gunmam in Siddha) and also for a wide variety of Abdominal conditions.[49]

Fever

Bone marrow aspiration/biopsy (BMA/B) has been described as a diagnostic tool in AIDS patients with fever of unknown origin (FUO). Tuberculosis, Aspergillosis, and Leishmaniasis the opportunistic infections diagnosed on BMA/B specimens. [62]

The most common BMA isolates in severely immunocompromised patients include *Mycobacterium avium/intracellulare (MAI), Mycobacterium tuberculosis (MTB)* and *Histoplasma capsulatum*, all of which have a propensity to disseminate and cause disease in patients with AIDS. A BMA examination can implicate a particular organism if certain histological features are seen on biopsy. Although granulomas and lymphohistiocytic aggregates can be non-specific findings, they have also been associated with *H capsulatum* and *Cryptococcus neoformans.* [63] A study also revealed that coralline hydroxyapatite particles loaded with medically active substances improved drug stabilization, higher drug encapsulation efficiency of the carrier and showed significant ability to control the growth of bacteria.[63]

Research report showed that Sangu parpam had analgesic, antipyretic and anti-inflammatory activity which may aid as febrifuge .[30]

2. CONCLUSION

Human immunodeficiency virus (HIV) infection is a global public health issue. Anti-HIV therapy involving chemical drugs has improved the life quality of HIV/AIDS patients. However, emergence of HIV drug resistance, side effects and the necessity for long-term anti-HIV treatment are the main reasons for failure of anti-HIV therapy. Therefore studies were carried out on Marine Anti-HIV agents, to prove their efficacy on HIV as stated in ancient litratures. These evidences suggest that marine-derived anti-HIV agents have potential as active ingredients for preparation of novel pharmaceutical products due to their valuable biological functions with beneficial health effects. Therefore, further research studies are needed in order to investigate their activities in-depth in human subjects.

Acknowledgement:
The author expresses her gratitude to Dr.R.Meena Kumari, Director –National Institute of Siddha, Ministry of AYUSH, Chennai-47 for constant encouragement, Monitoring, and guidance throughout the study.

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