

Applicability, Feasibility and Efficacy of Phytotherapy in Aquatic Animal Health Management

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Abstract

The use of chemotherapeutants, antibiotics, and pesticides in aqua farms and non-adherence to scientific management practices have resulted in adverse impact on aquacultural production, serious outbreaks of diseases, development of drug resistance in microbes, and accumulation of antibiotics and pesticide residues in finfish and shellfish and environmental pollution. As a result, a need has been felt by the aquaculturists as well as aquatic animal health management professionals to find a suitable alternative therapy in place of antibiotics and chemotherapy. Phytotherapy has come to be recognized as a handy and viable alternative to chemotherapy, as it is economical, effective, non-resistance forming, renewable, eco-friendly and farmer-friendly. Although the use of medicinal plants is known to humanity since the dawn of human civilization for the treatment and control of human and animal diseases but its importance in combating finfish and shellfish diseases has been realized only recently. The phytotherapy of aquacultural diseases is in its infancy in most part of the world except in China to some extent. However, many important contributions in this field by different workers during the last quarter of the 20th century and early 21st century have shown encouraging results and opened new vistas in phytotherapy of aquatic animals. The present review critically evaluates the present status of knowledge of phytotherapy in the world combating various aquacultural diseases, identifying the bottlenecks and suggests remedial measures.

Keywords

Phytotherapy, Finfish and Shellfish, Microbial and Parasitic Diseases in Aquaculture, Immunostimulants, Biopesticides

1. Introduction

Phytotherapy is the oldest form of healthcare known to mankind. It has been used for treatment of humans and animals since thousands of years. In fact, long before humans knew anything about diseases, plants knew how to treat them. Herbal treatment has been an integral part of the development of modern civilization. The knowledge of phytotherapy is built upon the experiences of several generations, often of several centuries, and the data upon which it is based have been often obtained at a price in human lives.

Medicinal plants are the treasures of our planet. In India the use of medicinal plants for treatment of various diseases and ailments dates back to the times of Rig Veda written between 4500-1600 B.C. Some of the legendary works on use of medicinal plants for treatment of various diseases were pioneered by great ancient Indian physicians like Sushrut, Charak, Chakradatta, Vagbhata, Vangsen, Bhavaprakasha etc. The Charak Samhita written at 1000 B.C. gives comprehensive details of therapeutic use of medicinal plants. In 2735 B.C., the Chinese emperor Shen Nung wrote an authoritative treatise on herbs that is still in use today. The records of King Hammurabi of Babylon (c.1800 B.C.) include instructions for using medicinal plants. In c.400 B.C. first Greek herbal was written and in c.100BC first illustrated herbal was produced in Greece. By c.50 A.D., Roman Empire spread herbal medicine and commerce of plants around the Empire. The entire Middle East has a rich history of herbal healing. There are texts surviving from the ancient cultures of Mesopotamia, Egypt, and India that describe and illustrate the use of many medicinal plant products. In the scriptural book of Ezekiel, which dates from the sixth century B.C., we find this admonition regarding plant life. By the seventeenth century, the knowledge of herbal medicine was widely disseminated throughout Europe. The first U.S. *Pharmacopeia* was published in 1820. This volume included an authoritative listing of herbal drugs, with descriptions of their properties, uses, dosages, and tests of purity. It was periodically revised and became the legal standard for medical compounds in 1906. In 1900s A.D. the BHMA produced the British Herbal Pharmacopoeia.

At present more than 25% of the prescribed modern medicines in the world are made from medicinal plants. The World Health Organization (WHO) estimates that 80% of the world's population living in developing countries of Asia, Africa and Latin America, still relies on herbal medicines as its major source of primary health care. There are over 750,000 plants on the planet earth. However, up till now, only 5% of the plants species have been screened for biological activity. India is one of the world's 12 leading biodiversity countries blessed with 16 agro-climatic zones, 45,000 different plant species and 15,000 medicinal plants that included 7000 plants sourced by Ayurveda, 700 by Unani medicine, 600 by Sidha, 450 by Homoeopathy and 30 by modern medicine. According to an all India ethnobiological survey carried out by the Ministry of Environment & Forests, Government of India, there are over 8000 species of medicinal plants being used by the people of India [1]. Despite accounting for only 2.5 per cent of the total land area, India houses over eight per cent of the recorded species.

Herbal medicine is a type of medicine that uses roots, stems, leaves, flowers, or seeds of plants to improve health, prevent disease, and treat illness. It includes herbs, herbal preparations and finished herbal products that contain as active ingredients, parts of plants, or other plant materials or combinations. The medicinal plants produce a large number of organic chemicals of high structural diversity which are called secondary metabolites. Some of them are produced for self-defense [2]. The secondary metabolites are divided into three different categories based on their mechanism of function, *i.e.*, chemotherapeutic, bacteriostatic, bactericidal, and antimicrobial [3]. The herbal extracts and herbal medicines are called “Rasayan” in Ayurvedic literature which have been used since time immemorial to treat and control numerous diseases of bacterial, viral, fungal and parasitic etiologies [4]-[11] like skin diseases, cough, cold, fever, headache, migraine, eye infections, respiratory tract infections, diarrhea, hepatotoxicity and anticancer, antistimulant, neurostimulant antiaging, antireumatic, adaptogenic, and antistress etc [12] [13] and a host of many other ailments [14] [15]. There are estimated to be around 25,000 effective plant based formulations are available in the indigenous medical texts in India and around 10,000 designed.

2. Health Challenges in Aquaculture

Disease, decay and death have always coexisted with life whether it is human, animal, fish or for that matter any organism. It is, therefore, imperative that treatments of diseases must also have been contemporaries with the dawn of human intellect. Like any animal including humans, fishes also suffer from a variety of diseases caused by pathogens and parasites viz. microbes including virus, bacteria and fungi; protozoan and metazoan parasites including helminths, nematodes, annelids, molluscs and arthropods. The infectious diseases account for 60% of the fish production loss in aquaculture ponds. Fishes are cold-blooded animals; consequently, they suffer from many environmental and stress-related diseases as well. Besides, there are many nutritional diseases also. The outbreak of diseases jeopardizes regular aquaculture and threatens aquaculture production. Because fish are schooling aquatic animals, they are hard to observe individually, making the diagnosis and treatment of disease difficult. Therefore, controlling disease is one of the most vital tasks in aquaculture. With ever increasing intensification, finfish and shellfish farming have suffered from serious outbreaks of diseases in the recent past. Unscientific management practices together with irrational use of synthetic (unnatural) chemicals and therapeutics have had disastrous implications on aquacultural production due to catastrophic outbreaks of diseases. Recently the world aquaculture has encountered two major dreaded diseases: (i) Epizootic Ulcerative Syndrome (EUS) in finfish and (ii) White Spot Syndrome virus (WSSV) in prawns. So catastrophic are these two diseases that they have endangered almost the majority of fish and prawns population and their survival itself is threatened [7] [8].

These diseases (together with many others) have led to tremendous produc-

tion and economic losses to fish farmers, aqua-entrepreneurs and fish workers whose livelihood entirely depended on aquaculture or related enterprise. Every year millions of dollars worth of finfish and shellfish produce are lost due to diseases worldwide.

Off late aquaculturists the world over have heavily relied on the use of antibiotics, synthetic drugs, chemotherapeutants and pesticides to combat the disease problems facing the aquaculture industry. In India itself fish farmers use a large number of pesticides like nuvan, malathion, eldrin, BHC, ekalux, cypermethrin, parathion, trichlorophon, diuron, etc. to control the ectoparasites of fish. Due to this, pesticide resistance and bioaccumulation of pesticide have also been noticed. Future is ominous for the connoisseurs of fish so much exposed to pesticides. The advocates of pesticides must realize that to argue that we must use pesticides to feed a growing population is like saying we need to feed you even if it means poisoning to death. Farmers have also resorted to reckless use of antibiotics in fish ponds. Due to this, large numbers of cases of antibiotic resistant strains of bacteria have come to light [16] [17] [18]. Germs are winning the war against diseases. Fish farmers are facing the challenge of drug resistant bacterial pathogens, which have stopped responding to most of the conventional antibiotics [19]. Besides, there is the problem of bioaccumulation of antibiotics in the fish body. Off late, several consignments of seafood mostly cultured shrimps exported from India have been rejected by many EU countries due to the presence of antibiotic residues in them resulting in considerable economic losses to the seafood exporters. Moreover treatment with antibiotics, pesticides or other sources of chemotherapy involves very high cost to the aqua-farmers and many times cost of medicine is higher than the cost of the fish to be saved.

In this grim situation, the aqua-farmers the world over have started searching for novel and effective alternative therapy from renewable resources. Phytotherapy has come as a handy and viable alternative to chemotherapy. Herbal medicines are effective, economic, eco-friendly and farmer friendly, easily biodegradable, non-habit forming, non-resistance forming, non-narcotic, and without much side effects. Besides, the raw materials are inexpensive, renewable, locally available, user friendly, and can be easily prepared [20].

3. Phytotherapy in Aquaculture

The application of Phytotherapy in field of fish and fisheries is a relatively new area of research which is still in its infancy. The rapid detection and identification of fish pathogens is crucial for successful disease control in an aquafarm. The herbs may be used in many ways such as garden fresh, dried, powdered, juices, or extracted (in various solvents like water, alcohol, acetone, ether, etc), or essential oils. The herbal medicines are applied either as decoctions (individual) or concoctions (mixed) or in combination with other drugs for effective fish health management [21]. In India, “Mrgayurveda”, a branch of Ayurveda deals with animal life and treatment of animal diseases by herbal medicines. One Indian plant that is most studied world wide, is *Azadirachta indica* A. Juss (syn.

Melia azadirachta). A cornerstone of the Ayurvedic tradition, neem is known as “*sarva roga nivarak*” or “healer of all ailments” in India. Not surprising, that the people of India regard neem tree as “*village pharmacy*”. United Nations has declared Neem as the “Tree of the 21st Century”. Its medicinal and pesticidal effects are well documented. Preliminary studies have revealed that water soluble part of alcoholic extract of *A. indica* leaves possessed hypoglycemic, hypolipidemic, hepatoprotective, antifertility, hypotensive and anti-serotonin activity [22] [23] [24] [25] [26]. Beside neem, many other herbs like turmeric (*Curcuma longa*), tulsi (*Ocimum sanctum*), garlic (*Allium sativum*), *Adhatoda vasica* [7] etc. have also been used to treat aquacultural diseases. Chinese system of phytotherapy is quite popular among Chinese fish farmers who have taken lead in herbal treatment of finfish and shellfish diseases in the Asian region.

Off late in China, use of antibiotics to prevent and cure aquacultural diseases, has been modified by addition of herbal medicines with feed or culture medium [27]. The fish farmers are using various Chinese herbal therapies to control diseases and getting good results. For example, in Zhejiang Province, *Euphorbia humifusa* and *Acalypha australis* are used for enteritis and in Guangdong Province, *Thysanospermum diffusum* is used to cure bacterial kidney disease, gill rot, and enteritis [28]. The Institute of Hydrology, Academia Sinica, China has reported promising results with the application of Chinese tallow tree (*Sapium sebiferum*) with Chinese rhubarb (*Rheum officinale*) for “white-head-and-white-mouth” disease and bacterial gill rot. For control of hemorrhagic septicemia in fish, decoction of Chinese rhubarb (*Liquidambar taiwaniana*) is given with feed for 5 consecutive days with successful results [28]. Erythroderma is a common disease of grass carp and black carp in China which is caused by *Pseudomonas fluorescens*. It has been found that Chinese gall (*Galla chinensis*) applied @ 2-4 ppm controls erythroderma [28]. Enteritis is also common among grass carp, black carp (*Mylopharyngodon piceus*), bighead (*Aristichthys nobilis*) and common carp which is believed to be caused by *Aeromonas hydrophila* f. *intestinalis*. The enteritis has been successfully controlled by the use of a number of herbal medicines mixed into feeds, they are as follows : (1) Decoction of Chinese gall @ 2 - 3 ppm, Garlic @ 1 - 2 kg/100g fish daily for 6 consecutive days; or (2) *Euphorbia australis* @ 500 g dry herb or 2.5 kg fresh herb for 100 kg fish daily for 3 consecutive days; or (3) *Acalypha australis*-500g dry herb or 2 kg fresh herb per 100 kg fish daily for 3 consecutive days; or (4) Water knotweed (*Polygonum hydropiper*)—500 g dry herb or 2 kg fresh herb for 100 kg fish once daily for 3 consecutive days; (5) *Andrographis paniculata*—2 kg dry herb or 3 kg fresh herb for 100 kg fish for 5 - 7 days; (6) Fresh *Portulaca oleracea* @ 1.5 - 3 kg/100kg fish; or (7) *Artemisia argyi* @ 100 g powder of *A. argyi* and *Polygonum hydropiper* 500 g powder or 1 kg fresh per 10,000 fingerlings; or fresh mock strawberry (*Duchesnea indica*) @ 1 kg/100kg fish [29]. Bacterial gill rot affects grass carp, black carp, bighead, common carp and other fishes; grass carp is the main victim. It has been successfully controlled by the use of following herbal medicines: (1) add dry powder of Chinese tallow tree (*Sapium sebiferum*) leaves to pond

water to a concentration of 6.25 ppm; (2) add powder of Chinese rhubarb (*Rheum officinale*) to pond to a concentration of 2.5 - 3.7 ppm; (3) add Chinese gall to pond to a concentration of 2 - 4 ppm; (4) spread a solution of maple leaves over the pond; and (5) add Chinese sweet gum:water @ 2:1 [28].

The fish farmers of Bangladesh practice a unique system of plant-based aquaculture wherein bamboo stems and branches, jute sticks, the remains of sugarcane stalks, and/or tree branches are used as substrate. The various stalks are inserted vertically into the pond bottom, where they are colonized by the plankton, microbes, invertebrates and other organisms that make up periphyton. Fish graze on these concentrated forms of food more efficiently and the periphyton mats improve the water quality of the pond [30]. In this system fish production of 2305 kg/ha could be achieved within 90 days using Indian major carps catla, *Catla catla*; rohu, *Labeo rohita*; and *L. calbasu* [31]. Similar practices have also been known in West Africa where it is called as *Acadja*, in Bangladesh it is known as *Katha*, and in Cambodia *Samarah* [32]. In fact, people of Nalbari district of Assam province of India use juice of betel nut and paan (locally known as Peek) for determining the quality of water with quite good results.

The various herbal-based therapeutic measures adopted for the treatment and control of different diseases of finfish and shellfish, and fish health management can be categorized as follows:

3.1. Antibacterial

Herbs are nature's own antibiotics. Many herbal medicines and medicinal plant extracts have been tried to treat and control the bacterial diseases and bacterial pathogens of finfish and shellfish. Dey and Chandra [33] showed that fry of Indian major carp, *Catla catla* when treated with 2% aqueous extract of an herbal formulation, were resistant to induced infection of *Aeromonas hydrophila*, and had higher neutrophil and lymphocyte counts than the untreated controls. Dey and Chandra [34] reported successful control of Epizootic Ulcerative Syndrome (EUS) in fish by applying turmeric and lime in affected fish ponds at 5 - 7 days intervals. Hota and Dey [35] studied the effect of turmeric (*Curcuma longa*) extract on some fish pathogenic bacteria and found that it has antibacterial effect on two important fish pathogens viz. *Aeromonas* and *Staphylococcus*. *C. longa* contains curcumene, tumerone, and turmerol. Its methanolic extract exhibits antibacterial activity against *Micrococcus luteus*, *Enterococci faecali*, and *Staphylococcus aureus* [36]. Curcuminoids and gingerols have been reported to have antimicrobial, antifungal, anti-inflammatory, and antioxidant activities [37], [38]. Its rhizome is used to cure pimples, whitening of skin, and also as blood purifier [39].

Chopra *et al.* [40] showed that oil from the leaves, seeds and bark of neem *Azadirachta indica* possesses a wide spectrum of antibacterial action against Gram-negative and Gram-positive microorganisms, including *M. tuberculosis* and streptomycin resistant strains. *In vitro* it inhibits *Vibrio cholerae*, *Klebsiella pneumoniae*, *M. tuberculosis* and *M. pyogenes* [41] [42] [43]. Antimicrobial ef-

fects of neem extract have been demonstrated against *Streptococcus mutans* and *S. faecalis*. Extracts from stem bark of neem *A. Indica* is active against *Klebsiella*, *Staphylococcus*, and *Serratia* species [44]. Nim 76, a product from neem oil showed inhibitory effect on the growth of various pathogens including bacteria, fungi and virus. Some of the bioactive compounds responsible for neem's antibacterial property are nimbidin [45], nimbin, nimbinin, nimbidinin, nimbidic acid [46], nimbolide [47] [48]; mahmoodin [49]; margolone, margolonone and isomargolonone [50]. Das *et al.* [51] tested Aquaneem, an emulsified product prepared from the neem against four pathogenic bacteria of fish viz. *Aeromonas hydrophila*, *Pseudomonas fluorescens*, *Escherichia coli* and *Myxobacteria* spp. and found that their growth were remarkably inhibited. Similar observations have been made by Sahu *et al.* [52] with aquaneem as effective fish bactericide. Das *et al.* [51] recommended 10 ppm of aquaneem for pond application in culture system for control of bacterial diseases of fish such as haemorrhagic septicaemia, fin rot and tail rot, bacterial gill disease and dropsy like conditions. The antibacterial herbal product extracted from *Solanum trilobum*, *Andrographis paniculata*, and *Psoralea corylifolia* bio-encapsulated in *Artemia* and fed to PL of *P. monodon* enhanced the survival rate of post larva when grown in water containing shrimp bacterial pathogen [53].

Xu *et al.* [54] reported that the aqueous extract of Chinese herbal medicines showed antibacterial activity against shrimp bacterial pathogens. Jin *et al.* [55] tested fifteen Chinese herbal medicines against *Vibrio harveyi* causative agent of skin ulcer disease in sea-perch out of which three herbal medicines from *Rhizoma sanguisorbae*, *Pericarpium granati* and *Frucus schizandrae* were most effective against the pathogenic bacteria. Sun *et al.* [56] conducted a comparative study on the impact of dietary furazolidon and a Chinese herbal medicine *Portulaca oleracea* L. in fat greenling (*Hexagrammos otakii*) affected with bacterial gill rot disease. They reported 90% survival in fishes fed with herbal medicine *Portulaca oleracea*, while those fed with furazolidon supplemented diet could achieve 65% survival. Shuming *et al.* [57] reported 85% cure from bacterial septicemia in *Carassius auratus* by applying Chinese herbal medicines composed of *Scutellaria baicalensis*, *Herba euphorbiae* applied @ 2% to 4%. Zheng *et al.* [58] tested the efficacy of 15 Chinese herbal medicines on *Vibrio alginolyticus*, a pathogen of vibriosis of large yellow croaker, *Pseudosciaena crocea* (Richardson) out of which 4 herbal medicines viz. *Pericarpium granati*, *Rhizoma sanguisorbae*, *Fructus schizandrae*, *Rheum officinale* were most effective.

Raman [7] has found remarkable antibacterial activity of Indian medicinal plant vasa (*Adhatoda vasica*) against *Pseudomonas fluorescens*, a virulent and ubiquitous fish pathogen involved in many bacterial diseases of fish. The Holy basil Tulsi (*Ocimum sanctum*) has also potent antimicrobial properties [59]. It inhibits the growth of *E. coli*, *B. anthracis*, *M. tuberculosis* [60]. It is useful in respiratory tract infection, bronchitis, chronic cough and gastric diseases of children. The Ursolic acid present in tulsi has anti-allergic properties. A variety

of biologically active compounds have been isolated from the tulsi leaves including ursolic acid, apigenin, eugenol and luteolin. The essential oil of tulsi also has antibacterial properties [61]. Its oil is rich in vitamin C, carotene, calcium and phosphorus. Immanuel *et al.* [62] reported that butanolic extracts of terrestrial herbs *Ricinus communis*, *Phyllanthus niruri*, *Leucus aspera*, *Manihot esculenta*; and sea weeds *Ulva lactuca* and *Sargassum wightii* when tested against shrimp pathogen *Vibrio parahaemolyticus*, and fed with herbal extracts enriched *Artemia*; boosted the survival, specific growth rate and also lowered *V. parahaemolyticus* load in muscle and hepatopancreas tissues of treated *Penaeus indicus* juveniles. Bhuvaneswari and Balasundaram [63] screened ethanolic extracts of *Acalypha indica*, *Acorus calamus*, *Coleus aromaticus*, *Heliotropium indicum*, and *Indigofera aspalathoides* for antibacterial activity against *Aeromonas hydrophila*. They found that *A. calamus* and *I. aspalathoides* warded off the growth of the pathogen completely at minimum inhibitory concentrations of 1.29 and 2.16 mg/l, respectively suggesting that herbs can replace antibiotics against bacterial infection in fish. Chakraborty *et al.* [64] have extracted compounds like labda-14-ene 3a, 8alpha-diol and labda-14ene-8alpha-hydroxy-3-one from sea lettuce *Ulva fasciata* which were inhibitory to the growth of marine aquacultural pathogen *Vibrio parahaemolyticus*.

Besides these herbs, there are large number other medicinal plants, which have been studied extensively for their antibacterial properties against human and animal pathogens and thus have promising value against pathogenic bacteria of fish and shellfish. Some important among them are as follows (Table 1). The list of antibacterial herbs is quite exhaustive to suffice in the limited space in this paper. These and other time tested medicinal plants could be evaluated against different bacterial pathogens of fish.

3.2. Antiviral

The viral diseases take heavy toll of finfish and shellfish stocks annually. Holy basil Tulsi (*Ocimum sanctum*) has antiviral properties [59]. Ayurvedic Tulsi preparations have significantly reduced the symptoms of viral hepatitis. Rao [84] made an attempt to treat white spot disease successfully with turmeric powder (*Curcuma longa*), *Phyllanthus neruri*, and *Clicanthus nutans*. Applying neem extract to the culture pond soil also minimized white spot disease outbreak [85]. Citarasu *et al.* [86] studied the effect of methanolic extracts of five Indian medicinal plants viz. *Cyanodon dactylon*, *Aegle marmelos*, *Tinospora cordifolia*, *Picrorhiza kurooa* and *Eclipta alba* on WSSV challenged *Penaeus monodon*. They observed that those shrimps which were not fed with this herbal diet (control), died within seven days upon challenge with WSSV, while those fed with herbal supplemented diets had 74% survival and reduction in viral load. Much work on antiviral effect of herbs in fish has not been carried out. However, the works done on medicinal plants against animal viruses may be investigated for application against viral pathogens of finfish and shellfish. Some important antiviral herbals are presented in Table 2.

Table 1. Antibacterial activity of some medicinal plants.

S. No.	Name of Plant	Name of Bacteria	Author
1	<i>Vitis adnata</i> (Essential oil)	<i>Salmonella pullorum</i>	Srivastava, 1996 [65]
2	<i>Cymbopogon citrates</i> (Oil)	<i>Shigella flexneri</i> , <i>E. coli</i> , <i>Staphylococcus aureus</i> , <i>Salmonella typhi</i> and <i>Klebsiella pneumoniae</i>	Syed <i>et al.</i> , 1995 [66]
3	<i>Chamaesyce hirta</i>	<i>S. flexneri</i>	Vijaya and Ananthan, 1996 [67]
4	<i>Ipomea fistulosa</i> (Ethanol extract)	<i>Streptococcus faecalis</i>	Chowdhury <i>et al.</i> , 1997 [68]
5	Cabbage juice	<i>S. aureus</i>	Kyung and Fleming, 1997 [69]
6	<i>Anacardium occidentale</i>	<i>S. aureus</i> and <i>Serratia marcescens</i>	Sathwane <i>et al.</i> 1997 [70]
7	Bhallatakasava and Sukshma Triphala	<i>Clostridium titani</i>	Kulkarni <i>et al.</i> , 1995 [71]
8	<i>Eucalyptus</i> oil	<i>Mycobacterium avium</i>	Leite <i>et al.</i> , 1998 [72]
9	<i>Centella asiatica</i>	<i>Bacillus subtilis</i> , <i>E. coli</i> , <i>P. aeruginosa</i> and <i>Pseudomonas cichorii</i>	Srivastava <i>et al.</i> , 1997 [73]
10	<i>Terminalia bellerica</i> , <i>Garcinea gummigulla</i> , <i>Anisomeles malabarica</i> , <i>Aegle marmelos</i> , <i>Alangium saluifolium</i> and <i>Zizyphus jujuba</i>	<i>B. subtilis</i> , <i>S. aureus</i> , <i>E. coli</i> and <i>P. aeruginosa</i>	Valsaraj <i>et al.</i> , 1997 [74]
11	<i>Azadirachta indica</i>	Wide spectrum antibacterial action against Gram-negative and Gram-positive microorganisms, including <i>M. tuberculosis</i> and streptomycin resistant strains.	Chopra <i>et al.</i> , 1952 [40]; Patel and Trivedi, 1962 [41]; Satyavati <i>et al.</i> , 1976 [42]; Ahmad <i>et al.</i> , 1995 [43]
12	<i>Ocimum sanctum</i>	<i>E. coli</i> , <i>B. anthracis</i> , <i>M. tuberculosis</i>	Bhargava, and Singh, 1981 [60]
13	<i>Gloriosa superb</i> (leaf extract)	<i>S. aureus</i> <i>B. subtilis</i> , <i>K. pneumoniae</i> and <i>E. coli</i>	Subashini <i>et al.</i> , 2000 [75]
14	Triphala churna, Hareetaki churna, Dashmula churna	<i>S. epidermidis</i> , <i>P. vulgaris</i> , <i>S. aureus</i> , <i>E. coli</i> , <i>P. aeruginosa</i> and <i>S. typhi</i> .	Tambekar and Dahikar, 2011 [76]
15	<i>Moringa oleifera</i> (leaf extract)	<i>B. cereus</i> , <i>B. subtilis</i> , <i>S. aureus</i> , <i>S. infea</i> and <i>M. phlei</i>	Pal <i>et al.</i> , 1995 [77]
16	<i>Calotropis procera</i> (Ethanol extract)	<i>Enterobacter cloacae</i> and <i>Fusarium moniliforme</i>	Jain, <i>et al.</i> , 1996 [78]
17	<i>Adhatoda vasica</i>	<i>Pseudomonas fluorescens</i>	Raman, 2004 [7]
18	<i>Pericarpium granati</i> , <i>Rhizoma sanguisorbae</i> , <i>Fructus schizandrae</i> , <i>Rheum officinale</i>	<i>Vibrio alginolyticus</i>	Zheng <i>et al.</i> , 2005 [58]
19	<i>Acorus calamus</i> and <i>Indigofera aspalathoides</i>	<i>Aeromonas hydrophila</i>	Bhuvanewari and Balasundaram, 2006 [63]
20	<i>Ulva fasciata</i>	<i>V. parahaemolyticus</i>	Chakraborty <i>et al.</i> , 2007 [64]
21	<i>Allium sativum</i>	<i>Aeromonas hydrophila</i> infection in Rohu fish <i>Labeo rohita</i>	Sahu <i>et al.</i> , 2007a [79]
22	<i>Magnifera indica</i> kernel	<i>Aeromonas hydrophila</i> infection in Rohu fish <i>Labeo rohita</i>	Sahu <i>et al.</i> , 2007b [80]
23	<i>Azadirachtin</i> from Neem <i>Azadirachta indica</i>	<i>Aeromonas hydrophila</i> infection in goldfish <i>Carassius auratus</i>	Kumar <i>et al.</i> , 2012a [81], 2012b [82], 2013 [83]

3.3. Antifungal

The use of synthetic fungicides to control fish diseases has been restricted due to their carcinogenicity, teratogenicity, high and acute toxicity, long degradation period and their effect on food and health hazards for human beings. In recent

Table 2. Antiviral activity of some medicinal plants.

S. No.	Name of Plant	Name of virus	Author
1	Neem extract	Vaccinia virus	Rao <i>et al.</i> , 1969 [87]
		Chikungemya and Measles Virus Coxsackie Virus	Gogati and Marathe, 1989 [88] Badam <i>et al.</i> , 1999 [89]
2	<i>Maclura cochinchinensis</i> , <i>Centella asiatica</i> , <i>Mangifera indica</i> , <i>Cynometra cloiselli</i> , <i>C. madagascariensis</i> , <i>Evonymopsis longipes</i> , <i>Ravensara retusa</i> and <i>Terminalia monoceros</i> <i>Acorus calamus</i> extracts	Herpes Simplex Virus	Bunyapraphatsara <i>et al.</i> , 1999 [90] Yoosook <i>et al.</i> , 1999 [91]
	Badam, 1995 [92]		
3	<i>Syzygium kurzi</i> , <i>S. megacarpum</i> (extract)	Encephalitis Causing Virus	Chandra <i>et al.</i> , 1998 [93]
4	<i>Scilla hyacinthiana</i> , <i>Dillemia pomifera</i> , <i>Smilax perfoliadour</i> and <i>Rosa osmastonii</i> (extract)	Semilike Forest Virus (SFV) and Ranikhet Diseases Virus (RDV)	Rana and Joshi, 1998 [94]
5	<i>Cyanodon dactylon</i> , <i>Aegle marmelos</i> , <i>Tinospora cordifolia</i> , <i>Picrorhiza kurooa</i> and <i>Eclipta alba</i>	WSSV challenged <i>Penaeus monodon</i>	Citarasu <i>et al.</i> (2006) [86]
7	<i>Ocimum sanctum</i> (extract)	Anti-viral property	Janssen <i>et al.</i> , 1989 [59]
8	<i>Geranium sanguineum</i> polyphenolic (extracts)	Various strains of Human, Avian and Equine Influenza Virus	Serkedjjeva, 1996 [95]
9	<i>Hyptianthera stricta</i> (Ethanollic extract)	Encephalomyocarditis and Japanese Encephalitis Virus	Saxena <i>et al.</i> , 1997 [96]
10	<i>Cyanodon dactylon</i> , <i>Aegle marmelos</i> , <i>Tinospora cordifolia</i> , <i>Picrorhiza kurooa</i> and <i>Eclipta alba</i> .	WSSV challenged <i>Penaeus monodon</i>	Citarasu <i>et al.</i> 2006 [86]
11	Anti-WSSV drugs (MP07X) derived from the marine plant and (TP22C) derived from terrestrial plant).	White spot syndrome virus (WSSV) infected <i>Litopenaeus vannamei</i>	Chakraborty and Ghosh, 2013 [97]
12	Anti-WSSV drug (TP22C) derived from terrestrial plants	White spot syndrome virus (WSSV) infected shrimp <i>Litopenaeus vannamei</i>	Ghosh and Chakraborty, 2013 [98]

years, many phyto-extracts have been used as fungicides for the control of various fungal pathogens of finfish and shellfish due to their high antifungal properties, nontoxic nature, easy availability at low cost and with no side effects. Xu *et al.* [54] reported that aqueous extract of a Chinese herb, *Fructus prunusis* showed promising results in inhibiting the growth of *Fusarium oxysporum* which caused black gill disease in *P. orientalis*. Auro-de-Ocampo and Jimenez [99] showed that the extracts of *Helenium quadridentatum* were quite effective in controlling saprolegniasis in fish. Followings are some of the important works carried out on the antifungal effect of medicinal plants, which may have significant value for controlling fungal pathogens of finfish and shellfish:

Extract of neem leaf, oil and seed kernel have been found highly effective against certain fungi including *Trichophyton*, *Epidermophyton*, *Micrsporium*, *Trichosporon*, *Geotircum* and *Candida* [100] [101] Hexane extract of neem leaves and its chromatographic fractions exhibited significant antifungal activity against deuteromyceteous fungal pathogen [102]. The bioactive compounds of neem responsible for antifungal property of neem have been found as nimbidin [103] gedunin [104] cyclic trisulphide and cyclic tetrasulphide [105] and 10-undecyn-1-01 [102]. The *Eucalyptus* oil has been observed to have significant antifungal activity. Butanol and ethyl acetate extracts of *Calotropis procera* was found highly effective against *Candida albicans* (Table 3).

Table 3. Antifungal activity of some medicinal plants.

S. No.	Name of Plant	Fungal Pathogens	Author
1	<i>Fructus prunusis</i>	Black gill disease in farm shrimp <i>P. orientalis</i> caused by <i>Fusarium oxysporum</i>	Xu <i>et al.</i> , 1993 [54]
2	<i>Helenium quadridentatum</i> (Extract)	Saprolegniasis in fish	Auro-de-Ocampo and Jimenez (1993) [99]
3	Neem leaf (Extract), oil and seed	Human fungi including <i>Trichophyton</i> , <i>Epidermophyton</i> , <i>Micrsporum</i> , <i>Trichosporon</i> , <i>Geotircum</i> and <i>Candida</i> Deuteromyceteous fungal	Khan and Wassilew, 1987 [100]; Biswas <i>et al.</i> , 2002 [101] Govindachari <i>et al.</i> ,1999 [102]
4	Turmeric and lime in affected culture ponds at 5-7 days duration.	EUS disease in fish.	Dey and Chandra, 1994. [33]
5	Garlic (2 kg) + Salt (2 kg) + CuSO ₄ (20 g) + KMnO ₄ (20 g) mixed into a paste form which is added in 30 - 50 litre of water and sprayed over pond surface of 1.33 ha area.	EUS disease in fish.	Goswami <i>et al.</i> , 2006 [106]
6	Turmeric oil	Dermatophytic fungi, <i>Trichophyton rubrum</i>	Apisariakul <i>et al.</i> , 1995 [107]
7	The essential oil from the leaves of <i>Chenopodium ambrosioides</i>	antimycotic activity against <i>Trychophyton mentagrophytes</i> and <i>Microsporium audouinii</i> at 50 ppm	Kishore <i>et al.</i> , 1996 [108]
8	Garlic clove extract	<i>Fusarium solani</i> .	Alice and Sivaprakasam, 1999 [109]
9	Leaf extract of <i>Bauhinia variegata</i>	<i>Aspergillus fumigatus</i> and <i>A. niger</i>	Sharma and Saxena, 1996 [109]
10	Methanolic extract of rhizome of <i>Nelumbo nucifera</i>	Potent antifungal and antiyeast activity.	Mukherjee <i>et al.</i> , 1995 [111]
11	<i>E. citriodora</i> , <i>E. dalrympleana</i> and <i>E. laveopinea</i> (Essential oil)	six Dermatophytes	Shahi <i>et al.</i> , 1999 [112]
12	<i>E. citriodora</i>	<i>Pyricularia grisea</i>	Mishra <i>et al.</i> , 1997 [113]

3.4. Antiprotozoal

Protozoan parasites are ubiquitous in fisheries world whether it is inland or marine. They take heavy toll of finfish and shellfish particularly during their early life cycle from egg to fry and fingerling stages. They also infect the adult stage but mortality is less frequent than the infant stage.

Dey and Chandra [34] reported successful control of Trichodinosis in the seed (fry) of Indian major carp, *Catla catla*. They reported a severe incidence of Trichodinosis in a catla fry population in some nursery ponds caused by a ciliate protozoa *Trichodina indica*. The prevalence of the infection was 60% - 70% of the fry population. The infection was on the general body surface and fins. They could control the infection by applying 1 ppm aqueous extract of garlic and 10 ppm common salt/ha/m water. Works done in Chinese aquaculture, reports that reproduction of *Trichodina* can be inhibited by adding 15 - 20 kg/mu of china-berry (*Melia azadirach*) leaves once a week. Sprinkling 25 - 30 kg/mu of a decoction of fresh chinaberry branches and leaves is also effective [28]. Oketch-Rabah *et al.* [114] isolated two antiprotozoal compounds namely mazanzagenin and nyasol from *Asparagus africanus* and found the nyasol potently inhibits the growth of *Leishmania major* and *Plasmodium falciparum*.

3.5. Anthelmintic

Helminthic worms are significant parasites of fish. The worms of the class monogenea are mostly ectoparasitic with no intermediate host involved in the life cycle while the digeneteans are endoparasitic with a life cycle involving at least one intermediate host. Nematodes are also parasitic in fish requiring at least one other host to complete their life cycle. Other important group of worms parasitizing the fish is *Acanthocephala*. In acanthocephalans at least one intermediate host is required to complete the life cycle.

Mitchell and Hoffman [115] reported that Kamala, an ancient anthelmintic herbal medicine fed at 0.1% of the diet for three days if dry rations are being fed, or up to seven days if wet rations are fed, removes adult cestodes and other worms from fishes. The dose prescribed is 1 g/kg (45 g/100 lb) of fish per day for 7 to 14 days [116]. Ayurvedic system of medicine prescribes that flower; fruit, twig, seed, pulp and oil of neem eliminate helminthiasis in animals [101]. According to Neeraja and Narayana [117] Neemol, an ethanol extract of neem seed kernels has been found very effective against cestode parasites in white leghorns. Jangde *et al.* [118] tested anthelmintic property of two plants viz. *Artemisia maritima* and *Butea frondosa* against *Haemonchus contortus* worms in bullock and found that aqueous extracts of both these plants are highly effective in immobilizing and killing of the worms. The combination of these plants further reduced motility and death time.

3.6. As Biopesticide

Several plant species have insecticidal and pesticidal property. Many of them are highly effective against metazoan ectoparasites. Rajasekaran *et al.* [119] reported that oil of Tulsi (*O. sanctum*) has been used as a potent anti-malarial drug. Essential oil of Tulsi has been reported to possess 100% larvicidal activity against the *Culex* mosquitoes. Its extracts have marked insecticidal activity against mosquitoes. It also has mosquito repellent properties.

Shaoqui [28] reports a novel method for control of lernaeasis of carps in China. Adding 400 kg/mu of fermented cow dung or pig manure or 100 - 150 kg/mu of distiller's dregs for every meter of water depth successfully controls lernaeasis in carp. The pine (*Pinus massoniana*) applied @ 20 kg per 1/15 ha water area, also controls Lernaeasis [29]. Recently, Tiwari *et al.* [120] reported that stems of banana plant put squarely in the fish pond with small amount of kerosene oil, controls aquatic insects in nursery ponds.

Neem (*Azadirachta indica*) is the classic example of biopesticide. It has been identified by WHO/UNEP as environmentally "powerful" natural pesticide. Vietmeyer [121] sees Neem as a tree solving global health problems. Off late several biopesticides made of neem, either singly or in combination with other plants, have hit the market; some notable among them are: Achook (Godrej Agrovet), Neem Gold (SPIC), Neem Guard (Akshay Chem), Neemark (West Coast Herbchem), Margocide (Monofix & Co.), Jawan crop protector (MCDA Agro), Field Marshal (Khetiwadi Corner), Wellgrow (ITC Ltd.), Neemol (Meen-

al Oil & Agro Industries), Nethrin (Amitul Agrochem), Sukrina (Conster Pvt. Ltd.), Aquaneem, Neemta 2100, Nimin etc. Srinivasan *et al.* [122] tested, neem products like “Neem Azal”, “Nimbecidine”, “Neem Gold” against whitefly, *Bemisia tabaci* and reported that all neem products gave effective control against whitefly. Paruthi *et al.* [123] tested a neem based pesticide called “Achook” against root-knot nematode, *Meloidogyne incognita* and observed 90.7% reduction in larval hatch at 1.0 percent concentration. Clinical studies with the dried neem leaf-extract indicate its effectiveness to cure ringworm and eczema and scabies [101]. In an experiment to test the molluscicidal property of neem based pesticide like achook, nimbecidine and azadirachtin against snails *Lymnaea acuminata* and *Indoplanorbis exustus*, Singh *et al.* [124] observed that molluscicidal effect was time and dose dependent. The toxic effect of azadirachtin against both snails was greater than synthetic molluscicides. Recently, Kumar *et al.* [81] [82] tested effect of Azadirachtin on Argulus parasites of ornamental fish *Carassius auratus* and found that Azadirachtin @ 15 ppm is very effective in killing the *Argulus* spp. Similarly, Kumar *et al.* [125] tested Piperine on *Argulus* spp. parasites on *Carassius auratus* and reported 100% killing of these parasites with piperine @ 5 ppm. Osuala and Okwousa [126] found that neem stem bark extract was lethal against three common snails *Biomphalaria pfeifferi*, *Bulinus truncatus* and *Lymnaea natalensis*. Bail *et al.* [127] also screened some of the medicinal plants for their molluscicidal activity against snails. Dimetry and El-Hawary [128] tested a product from neem seed kernel called “Neem Azal-F” against aphid *Aphis craccivora* and found that the product inhibited the growth and reproduction of the aphids. Ganapragasam *et al.* [129] tested a neem-based pesticide called “Jawan” against some nematode pests and reported 100 percent kill at 10 - 20 dilution of the product. In an experiment on combined effect of curcumin (from turmeric) and l-cysteine, nemicidine, nemol and vimicidine (all from neem), Gangopadhyay [130] reported significant antifungal and insect repellent activity.

Beside neem, several other plants like cedar *Cedrus deodar*, *Pongamia* sp., *Eucalyptus* sp., *Acorus* sp., garlic (*Allium sativum*), ginger (*Zingiber officinale*), *Dialium guineense*, *Nerium indicum*, mahua oil, Karanj oil, *Momordica charantia*, *Pandanus odoratus*, camphor (*Cinnamomum camphora*), *C. zeylanicum*, *Syzygium aromaticum*, *Cymbopogon citratus*, *Derris* sp., *Annona muricata*, *Jatropha elliptica*, *Renealmia exaltata*, *Chenopodium ambrosioides*, *Ruta chalepensis*, *Vaccaria pyramidata*, *Thevetia peruviana*, *Ocimum* spp. etc, have significant insecticidal and pesticidal properties (Table 4).

3.7. As Immunostimulant

The use of immunostimulant in aquaculture has opened a new vista in fish health protection. It has proved to be an effective means of increasing immunopotency of fish. So far, a large number of immunostimulants, that include a very heterogeneous group of substances like synthetic chemicals, biological substances, mycelial fungi, killed mycobacterium, polysaccharides, glucans, peptidoglycan,

Table 4. Herbs as biopesticide.

S. No.	Name of biopesticide/plant	Effect	Author
1	Neem Azal, Nimbecidine, Neem Gold	Toxic to whitefly, <i>Bemisia tabaci</i>	Srinivasan <i>et al.</i> , 2001 [122]
2	Neem Azal-T/S	Toxic to <i>Gambusia affinis</i>	El-shazly and El-sharnoubi, 2000 [131]
3	Neem Azal-F	Toxic to Aphid, <i>Aphis craccivora</i>	Dimetry and El-Hawary, 1995 [128]
4	Achook (neem based pesticide)	Toxic to Root-knot nematode <i>Meloidogyne incognita</i>	Paruthi <i>et al.</i> , 1996 [123]
5	Neem leaf-extract	Kills Ringworm, Eczema and Scabies	Biswas <i>et al.</i> , 2002 [101]
6	Achook, Nimbecidine and Azadirachtin	Kills snails <i>Lymnaea acuminata</i> and <i>Indoplanorbis exustus</i>	Singh <i>et al.</i> , 1996 [132]
7	Neem stem bark extract	Kills snails <i>Biomphalaria pfeifferi</i> , <i>Bulinus truncatus</i> and <i>Lymnaea natalensis</i>	Osuala and Okwousa, 1993 [126]
8	Neem-based pesticide "Jawan"	Toxic to Nematode pests	Ganapragasam <i>et al.</i> , 1993 [129]
9	l-cysteine, nemicidine, nemol and vimicidine (derived from neem plant)	Antifungal and Insect Repellent	Gangopadhyay, 1995 [130]
10	Azadirachtin derived from Neem <i>Azadirachta indica</i>	<i>Argulus</i> parasite of goldfish <i>Carassius auratus</i>	Kumar <i>et al.</i> , 2012 [81] Kumar <i>et al.</i> , 2013 [82]
10	Curcumin (derived from turmeric)	Antifungal and Insect Repellent	Gangopadhyay, 1995 [130]
11	Rotenone (derived from Derris root)	Erdication of unwanted fish, affects respiratory system, fatal.	Medda <i>et al.</i> , 1995 [133]
12	<i>Croton tiglium</i>	Piscicidal	Babu, 1965 [134]
13	<i>Milletia pachycarpa</i>	Piscicidal	Bhuyan, 1968 [135]
14	<i>Justicia hayatai</i>	Fish poison	Ohta <i>et al.</i> , 1969 [136]
15	<i>Barringtonia acutangula</i>	Fish poison	Chakraborty <i>et al.</i> , 1972 [137]
16	<i>Randia dumetorum</i>	Fish poison	Nandy and Chakraborty, 1976 [138]
17	<i>Marchantia polymorpha</i>	Piscicidal	Kanasaki and Ohta, 1976 [139]
18	<i>Zanthoxylum armatum</i> fruits	Piscicidal	Ramanujam and Ratha, 1980 [140]
19	<i>Mahua oil cake</i>	Piscicidal	Bhatia, 1970 [141]
20	Logs of <i>Pala</i> and bamboo plants immersed in pond water	Controls fish lice (<i>Argulus</i> spp.)	Goswami <i>et al.</i> , 2006 [106]
21	Piperine derived from <i>Piper longum</i>	<i>Argulus</i> parasite of goldfish <i>Carassius auratus</i>	Kumar Abhay <i>et al.</i> , 2012 [125]

peptides, muramyl dipeptide, nutritional factors, hormones, cytokinins, and animal and plant extracts/ingredients like Azadirachtin, Piperine, Curcumin, *Ocimum sanctum*, *Aloe vera* extracts etc have been tested on the immune response in a variety of finfish and shellfish species [142] [143] [144]. However, the knowledge on the use of plant extracts and herbal medicines as immunostimulants is in its infancy, even though such botanical products are a rich source of active substances for immunotherapy [145].

Herbal drugs are known to possess immunomodulatory properties and generally act by stimulating both specific and non-specific immunity [146] [147] [148]. Many plants used in traditional medicine are reported to have immunomodulating activities. Some of these stimulate both humoral and cell mediated immunity while others activate only the cellular components of the immune

system, *i.e.* phagocytic function without affecting the humoral or cell mediated immunity [149] [150]. Scores of medicinal herbs have been tested and tried with good results, in the control of different diseases of fish and shellfish [151] [152]. In the past few years the medicinal plants investigated for their immunostimulatory response on fish include *Ocimum sanctum*, *Acalypha indica*, *Phyllanthus niruri*, *Phyllanthus emblica*, *Azadirachta indica*, *Crossandra infundibuliformis*, *Aloe vera*, *Curcuma longa*, *Solanum trilobatum*, *Piper betle*, *Murraya koenigi*, and *Mentha piperita* [153], turmeric [20]; Chinese herbs *Astragalus membranaceus*, *Polygonum multiflorum*, *Isatis tinctoria*, *Glycyrrhiza glabra*, *Lonicera japonica* [154] [155], *Massa medicata*, *Crataegi fructus*, *Scutellaria baicalensis*, *Artemisia capillaries*, *Cnidium officinale* [156].

The immunomodulatory properties of Holi Basil, Tulsi (*O. sanctum*) have been studied in detail by many workers [157] [158] [159] [160], Das *et al.* [144]. The leaf of *O. sanctum* contains water soluble phenolic compounds, and various other constituents such as eugenol, methyl eugenol and caryophyllene [23] that might act as a potential immunostimulant. Essential oil of *Ocimum sanctum* was found to have anti-allergic properties. When administered to laboratory animals, the compound was found to inhibit mast cell degranulation and histamine release in the presence of allergen. These studies reveal the potential role of *O. sanctum* extracts in the management of immunological disorders including allergies and asthma. It is also anti-inflammatory due to the eugenol present in the leaves. Venkatalakshmi and Dinakaran Michael [159] have reported that active ingredients of leaves of Tulsi are responsible for antibody response and promote nonspecific defense mechanisms. Working on immunostimulatory effect of *Ocimum sanctum*, Dinakaran [153] observed that frozen, lyophilized and sodium benzoate preserved leaf extract of *Ocimum sanctum* enhanced antibody response to *Aeromonas hydrophila* while the sodium benzoate preserved extracts enhanced neutrophil activity in Tilapia [159] [160]. The protective ability of *O. sanctum* is mediated through both specific and non-specific immune mechanisms, as evident from the enhanced antibody production and enhanced activation of neutrophils.

Turmeric also has several components with immunomodulatory and antioxidant properties [161] [162]. Immunostimulatory activity of neem (*Azadirachta indica*) has also been widely studied. The neem has been found to enhance immune response in healthy rats [163] [164], mice [165] [166] and immunocompromised hen [167]. Logambal and Michael [168] reported that *A. indica* enhances primary and secondary immune response in Tilapia *Oreochromis mossambicus*. The aqueous extract of neem leaf possesses potent immunostimulant activity as evidenced by both humoral and cell-mediated responses [169] [170]. Neem oil has also been shown to possess immunostimulant activity by selectively activating cell-mediated immune mechanisms to elicit an enhanced response to subsequent mitogenic or antigenic challenge. Kiran Kumar [171] studied the immunostimulatory effect of *Catheranthus roseus*, *Calotropis gigantea* and *Datura stromoneum* on *Cyprinus carpio* and found that *C. roseus* was more im-

munostimulatory followed *C. gigantea* and *D. stromoneum*. Rao and Chakrabarti [172], Chakravarti and Rao [173], Rao *et al.* [174] [175] have made a detailed study on the effect of dietary supplementation of *Achyranthes aspera* (family: Amaranthaceae) on the immunological response, antigen clearance and survivality of Indian major carps and found that *Achyranthes aspera* stimulates immunity and increases resistance to infection.

Chuntao *et al.* [154] studied the response of a herbal immunoregulation mixture (HIRM) comprising of extracts of the following traditional Chinese medicines (TCMs): *Astragalus membranaceus*, *Polygonum multiflorum*, *Isatis tinctoria*, *Glycyrrhiza glabra*. The results showed that, compared with those in the control group, the diets with 0.5% and 1% HIRM resulted in significant increase in macrophage phagocytic activity, macrophage ROS and the levels of total protein, globulin, albumin and NOS activity in serum indicating that the herbal mixture elevated the immunity in carp (*Cyprinus carpio*). Seung-Cheol *et al.* [156] studied the effects of dietary medicinal herbs: *Massa medicata*, *Crataegi fructus*, *Artemisia capillaries*, *Cnidium officinale*, and a mixture of all the herbs, on growth and non-specific immunity in juvenile red sea bream *Pagrus major*. The results revealed that medicinal herbs and herbal mixture enhanced the growth and non-specific immunity of red sea bream. Ardo *et al.* [155] studied the impact of Chinese herbs *Astragalus membranaceus* and *Lonicera japonica* extracts on the immune response of Nile tilapia (*Oreochromis niloticus*) challenged with *Aeromonas hydrophila* and observed that these herbs enhanced the immune response and disease resistance of cultured fish.

Although, these and many other plant extracts have been used as immunostimulants in fish, further studies are required to be conducted to find out the exact active ingredients responsible, and their mode of action. Further, most of the immunostimulants have been used mainly against bacterial diseases, the role of these immunostimulants against viral pathogens of finfish and shellfish is still not clear. Siwicki *et al.* [176] has stated that the best way of administration of immunostimulants to farm grown fish is to incorporate them in feed. **Table 5** summarises various immunostimulants and its impact on aquatic animals.

3.8. As Nutraceuticals

Many herbs incorporated with regular diets of fish have shown better growth and help in minimizing the onset of diseases. Dey and Chandra [34] reported to have raised disease resistant fry of Indian major carp, *Catla catla* through treatment with 2% aqueous extract of a herbal formulation. Treated spawn had better growth during 35 days of rearing, better survival, higher food consumption and better health status than untreated controls. Kavitha [189] demonstrated impact of herbs Satavari (*Asparagus racemosus*) and Chandrasoor (*Lepidium sativum*) @ 2 g/kg fish/day in promoting growth in Indian major carp *Labeo rohita*. Kumar [190] reported Ashwagandha (*Withania somnifera*) applied @ 0.08 g/kg fish/day in the diet of mrigal (*Cirrhinus mrigala*) resulted in a weight gain of 45.14%. In subsequent studies Mulethi (*Glycyrrhiza glabra* Linn.) and Kali musli (*Curculigo*

Table 5. Herbs as immunostimulant.

S. No.	Name of Plant/product	Type of Immunostimulatory activity	Author
1	Glycyrrhizin (Glycosylated saponin)	Anti-inflammatory, anti-tumour and immunostimulatory activities.	Wada <i>et al.</i> , 1987 [177]
2	Glycyrrhizin	Increased protection in yellowtail fish against <i>E. seriola</i> infection.	Edahiro <i>et al.</i> 1990, 1991 [178] [179]
3	<i>in vitro</i> treatment with glycyrrhizin	Enhanced respiratory burst activity of macrophages and proliferative responses of lymphocytes from rainbow trout.	Jang <i>et al.</i> , 1995 [180]
4	Rainbow trout treated orally with soyabean protein	Increased leucocyte activities such as phagocytosis, bacterial killing and production of superoxide.	Rumsey <i>et al.</i> , 1994 [181]
5	The bath administration of saponin with <i>Y. ruckeri</i> vaccine	Enhanced the <i>in vitro</i> bactericidal activities in rainbow trout.	Grayson <i>et al.</i> , 1987 [182]
6	The oral administration of saponin	Increased leucocyte migration in yellowtail.	Ninomiya <i>et al.</i> , 1995 [183]
7	Immunostimulant effect of <i>Spirulina</i>	Tilapia , Channel catfish Atlantic salmon.	Park and Jeong, 1996 [184]; Duncan and Klesius, 1996 [185] Gildberg <i>et al.</i> , 1996 [186]
8	Immunostimulant effect of <i>Ocimum sanctum</i> leaf extract <i>Azadirachta indica</i> , <i>Piper betle</i> , <i>Crossandra infundibuliformis</i> Sodium benzoate preserved extracts	Enhanced antibody response to <i>Aeromonas hydrophila</i> . Increase in antibody response and increase in neutrophil activity in <i>Oreochromis mossambicus</i> Enhanced neutrophil activity in Tilapia.	Dinakaran, 2001 [187] Dinakaran, 2001 [187] Venkatalakshmi and Dinakaran Michael, 2001 [159]
9	Acetone extract of <i>Phyllanthus niruri</i> , <i>Ocimum sanctum</i> and <i>Acalypha indica</i>	Enhanced the antiSRBC antibody response in Tilapia.	Hemapriya, 1997 [188]
10	<i>Catheranthus roseus</i> , <i>Calotropis gigantea</i> and <i>Datura stromoneum</i> .	Immunostimulatory effect on <i>Cyprinus carpio</i> .	Kiran Kumar, 2001 [171]
11	Aqueous extract of neem stem bark	Enhance immune response of Balb-c mice to sheep red blood cells.	Nirjo and Kofi-Tsekpoo, 1999 [44]
12	Aqueous extract of neem leaf	Potent immunostimulant activity humoral and cell- both mediated responses.	Sen <i>et al.</i> , 1993 [163]; Ray <i>et al.</i> , 1996 [165]
13	Leaf extract of neem	Higher IgM and IgG levels along with increased titer of antioalbumin antibody.	Ray <i>et al.</i> , 1996 [165]
14	Neem oil	Activate cell-mediated immune mechanisms to elicit an enhanced response to subsequent mitogenic or antigenic challenge.	Upadhyay <i>et al.</i> , 1993 [166]
15	<i>Achyranthes aspera</i>	Stimulates immunity and increases resistance to infection in Indian major carps.	Chakrabarti, R. and Y.V. Rao (2006). [173]
16	Holy basil, Tulsi <i>Ocimum sanctum</i>	Enhanced immunostimulatory action in Rohu fish <i>Labeo rohita</i> .	Das <i>et al.</i> , 2013 [144]

orchioides Gaertn.) @ 0.06 g/kg fish/day showed better growth in mrigal [191]. Kour [192] used the herb Bala (*Sida cordifolia*) as experimental feed and noticed significant increase in the growth of mrigal. Similarly, Singh [193] showed that growth of mrigal went up by the application of Makhana (*Euryale ferox* Salisb.). Similar attempts were made by [194] [195] on carps using Gokhru (*Pedalium murex* Linn.) and Lotus (*Nelumbium speciosum* Wild.) seeds respectively with encouraging results. Recently, Sharma *et al.* [196] showed that common carp

(*Cyprinus carpio communis* L.) fed with a conventional diet (groundnut cake and rice bran @ 1:1) mixed with a herb Kaunch (*Mucuna pruriens*) seeds powder @ 0.06 g/kg body weight/day exhibited better growth of 31.94% in comparison with control (14.28%). The results show that these herbs could be tried as feed supplements and as nutraceuticals in commercial aquaculture; however, further works are required to know as to how these herbs help in restoring fish health.

4. Future Research Prospects

Medicinal plants are nature's unique gift to mankind. Recognizing the tremendous importance of herbal sector in primary health care, the World Health Organization had launched its first ever comprehensive traditional medicine strategy in 2002. The strategy is designed to assist countries to develop national policies on the evaluation and regulation of herbal practices; create a stronger evidence base on the safety, efficacy and quality of the herbal products and practices; ensure availability and affordability of phytotherapy including essential herbal medicines; promote therapeutically sound use of TM/CAM by providers and consumers; and documentation of traditional medicines and remedies.

Modern medicine faces the challenge of developing safer and more effective therapeutics. Although crude extracts from various parts of plants have been used as medicine from time immemorial, modern drugs from these extracts can be developed only after extensive investigation of their bioactive mechanisms of action, pharmacotherapeutics, toxicity, and after proper standardization in clinical trials. The bioactive natural products are important source of drug leads, but most of the times their modes of action are unknown. Thus, elucidation of their physiological targets is essential for understanding their therapeutic effects [197]. Besides, discovery of novel targets of these clinically proven compounds may also suggest new therapeutic applications. Although, considerable works have been done in the investigation of novel chemotypes and pharmacophores from many medicinal plants, but still remain a meager 5% of the total plant known to mankind, while the potential of marine and aquatic plants has barely been tapped. Very little work has been done on the biological activity and plausible medicinal application of plants in combating the numerous diseases facing the aquaculture industry. As the global scenario is now changing towards the use of nontoxic plant products, the development of modern phytochemicals and drugs from medicinal plants is the need of the time to control various fish diseases problems. Hence, more serious investigations are required to harness the therapeutic properties of medicinal plants to combat disease problems in aquaculture. Greater emphasis has to be directed towards research on herbal formulations and drug development. The fisheries fraternity has to learn a lot from the work carried out on phytotherapy of human and other animal diseases and apply the suitable principles in combating the diseases of fisheries world.

The rising commercial demand for wild-source plant drugs in many countries is occurring against a backdrop of rapid deforestation and degradation of species-rich forest ecosystems [198]. Over two-thirds of the 50,000 medicinal plants

in use are still harvested from the wild. It is estimated that between 4000 and 10,000 of medicinal plants are now threatened or endangered. In India alone, more than 150 species have been categorized as endangered. The Convention on Biodiversity (CBD) and the Intellectual Property Rights (IPR) have laid down guidelines for the protection of a country's genetic resources. It is high time that all the stake holders related to herbal medicine production, trade and utilization must adhere to the conservation of biological diversity, the sustainable use of its components and the fair and equitable sharing of the benefits arising out of the utilization of these precious genetic resources.

An integrated approach to promote herbal medicines and medicinal plants, right from the stage of cultivation, collection, storage, processing and marketing in an organized manner with the help of leading pharmaceutical companies is needed. Systematic cultivation of medicinal herbs on a large scale by private entrepreneurs with positive support and incentives from government organizations needs to be explored.

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