by suppressing free radicals, enhancing prostaglandin synthesis and mucus secretion, which contributes to the healing process of stomach ulcers.

In our study, the goal is to develop another dosage form based on the localized medicinal plant Momordica charantia L. cultivated in the Bukhara region of the Republic of Uzbekistan. To obtain the necessary information on the study of antimicrobial and antihelicobacteric activity of medicinal plants from various types of raw materials and chemical components, an analysis of the scientific literature on the research topic was carried out and further directions of our research were identified.

MYCOBACTERIUM MARINUM IN FISH AND HUMANS

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Fish mycobacteriosis is a chronic progressive disease caused by ubiquitous acid-fast bacilli, identified as *Nontubercolous mycobacteria* (NTM). NTM could be classified into slowly and rapidly growing mycobacteria, where Mycobacterium marinum is affiliated to the first class. *Mycobacterium marinum*, *M. fortuitum and M. chelonae* are among the most identified NTM mycobacterial species associated with fish mycobacteriosis. Piscine mycobacteriosis is a common disease of marine, brackish and freshwater fish infecting more than 200 species of freshwater and marine fish in a vast region extending from the subarctic zone to the tropical one. This disease also infects tropical aquarium fish and is considered a major cause of morbidity and mortality in free-living fish. *Mycobacterium marinum* is an environmental, aerobic waterborne bacterium, belonging to photochromogenic Group I non-tuberculous *Mycobacteria* according to Runyon's classification. *M. marinum* is one of the most common atypical *Mycobacteria* that cause human opportunistic infection. It is considered as the most important fish pathogen, associated with multiple symptoms, e.g. uncoordinated swimming, abdominal swelling, loss of weight, skin ulceration, white nodule formation as granuloma in liver, kidney, spleen in both fresh and marine water fish. *M. marinum* is an ubiquitous waterborne bacterium with an optimal growth temperature around 30°C, which causes the infection of bats, fish, mice and amphibians after its inoculation. Experimental infection of mice with *M. marinum* at a temperature below 30°C developed pulmonary lesions, but not at 34°C. *M. marinum* is prevalent all over the world in marine water, brackish water, and fresh water and naturally infects more than 150 species of fish, frog, freshwater eels and oyster. In Africa, *M. marinum* has been isolated from normal humans' skin and also from soil. It grows on Lowenstein-Jensen media at 30 °C within duration of 2-3 weeks.

Mycobacterium sp. have been identified as one of the most important micro-organisms causing morbidity and mortality in cultivated and wild fishes all over the world. It has been recorded in fresh water and marine fish in the tropical and subarctic

regions. The cultured water fish species including sea bass and striped bass, the *Oreochromis mossambicus* fish and freshwater fishes belonging to the families *Anabantidae, Characidae and Cyprinidae* are considered especially susceptible to the infection with *Mycobacterium*. A case of *Mycobacterium marinum* infection was described in a farm of hybrid striped bass in Italy. This species was considered as a potential source of infections for humans during sport activities and also a hazard risk for workers in the fish farm. The economic effect of mycobacteriosis in fish industry is still underestimated owing to the long incubation period, chronic nature and difficult diagnosis particularly at the early infection stage. *M. marinum* was the most prevalent species causing sturgeon mycobacteriosis as evidenced by PCR-denaturing gradient gel electrophoresis and library sequencing of rpoB gene. Fish acquire the mycobacteriosis infection through the consumption of contaminated food and polluted water. Transovarian transmission was also recorded in viviparous fish and in live bearing fishes. The vertical transmission of mycobacteria was previously explained, although this transmission route has not been documented in salmonids. Zebra fish embryos were infected with *M. marinum* via bath exposure, while adult zebra fish were infected through the gut rather than gills via gavage and bath exposure. In summary, the disease is transmitted through skin injuries and the external bacteria are included in the cutaneous transmission route. Aquatic vertebrates as frogs and turtles are sources for fish infection with mycobacteriosis. Also, snails are believed to be an important reservoir in aquarium fish. Additionally, water fleas were also reported as source of *M. marinum* infection when aquarium fish fed on water fleas harboring this pathogen. Similarly it has been reported that contaminated water fleas are responsible for producing characteristic granulomata of fish mycobacteriosis in Siamese fighting fish, when they were used as a source of live food for rearing this fish.

M. marinum causes chronic, progressive disease of Zebra fish in a dose-dependent fashion. The induced tuberculosis in the zebra fish is similar to active human tuberculosis, where the predominant lesion at late stages from the infection are the presence of necrotizing granulomas, hallmark lesion of active tuberculosis with abundant bacteria in the necrotic areas. Acute infection was characterized by uncontrolled development of the pathogen and death of all fish within 16 days, while chronic infections were marked by the formation of granuloma in different organs and longer survival in the range of 4-8 weeks.

M. marinum-induced tuberculosis in adult zebra fish; most of zebrafish died within 2 weeks of infection with 8970 bacteria, while infection with 5 CFU caused 44% mortality and infection with 60 CFU caused 83% mortality by 16 weeks. The infected fish showed a reduction in feed intake and weakened swimming for 1 week during the period prior to death. The infected fish either remained listless at the bottom or at the surface, constantly opening and closing their mouths to increase the gas exchange. The dying fish were often marked with external red lesions on the trunk ventral to the lateral line, an exophthalmia with ascites in close proximity to internal organs, where the former two signs are indicators for osmoregulatory stress and kidney failure. Histopathological examinations mostly demonstrate a nonspecific

inflammatory infiltration of epithelioid cells, lymphocytes and Langhan's giant cells without caseation. The early lesions commonly reveal a collection of polymorphonuclear cells surrounded with histiocytes. The histopathological examination might be significantly consolidated by the rapidly improving possibilities of vivo imaging, such as magnetic resonance spectroscopic, microscopic techniques or even two-photon microscopy, tomography and high-resolution ultrasound.

M. marinum penetrates the skin via minor traumata arising from resting the elbows on the border of the fish pond. Nowadays, the exposure of swimmers to mycobacteria was reduced due to the chlorination of water in the swimming. The growth of *M. marinum* increased in a Swedish dolphin atrium due to the decrease of water chlorination. It has coincided with numerous animals acquiring cutaneous and subcutaneous *M. marinum* infection. Additionally, infection may be acquired by handling shellfish or fish or following trauma attributable to infected foreign bodies for instance wood splints.

The disease is not transmittable from person to person. Currently, most human infection cases happen with the exposure to aquaria as well as skin injuries occurring during the processing or preparations of seafood. The current practices of sanitary chlorination restrict largely the outbreaks of mycobacterial infections. The terms ‘fish tank granuloma’ and ‘fish handler's disease’ is often used due to the relation between home aquariums and the water-associated activities including swimming, fishing and boating.

M. marinum infections may have occupational hazards for pet shop workers. Many infections take place in fish fanciers who maintain the aquarium at home producing what is called fish fanciers “finger syndrome”. Some mycobacterial infection may take place through direct injury from fins of fish or bites, but most infections are acquired during aquarium handling, e.g. cleaning or water changing. The incubation period of *M. marinum* infection in humans ranges between 3 weeks and 9 months.

The evidence of zoonotic transmission of *M. marinum* had been formerly confirmed through studying the genetic linkages of isolates from both human and fish sources using pulsed field gel electrophoresis and amplified fragment length polymorphism. However, in one human clinical case, *M. marinum* was inoculated through a fish spine injury. Zoonotic infection had been ascribed to mycolactone toxin produced by mycobacteria. Although it is assumed that the local aquaculture industry is not the source of human infections in combination with the lack of records of human infections by some strains, but still only certain strains of *M. marinum* have zoonotic potential.

Mycobacterial infections may be either painful or painless, but it may be life threatening. Infections with *M. marinum* may be hypothetically classified into four clinical categories to help guide therapeutic options. Type I *M. marinum* is commonly observed in immunocompetent patients and known as single or limited lesions marked by superficial cutaneous infection, appearing in forms of crusted or ulcerated nodules

or verrucous plaques. These single lesions develop within weeks or months of contact with infected fish.

Piscine mycobacteriosis arising from *M. marinum* infection can have adverse effects on the fish of fresh water, marine and brackish water, constituting zoonotic implications. The data on the pathogenesis and virulence factors of *M. marinum* are still scarce and questionable. Further studies are required to trace the immune defense responses against *M. marinum* infection in fish. Prophylaxis and vaccine development are extremely important to protect different aquaria from *M. marinum* infection. The advent of molecular diagnostic tools and advanced epidemiological studies on fish mycobacteriosis can enhance our understanding of the strategic plans designed for controlling such disease. Due to its communicable public health hazard, the disease should be cautiously avoided by voiding swimming in fish pools and wearing gloves during handling and processing of fish. Future studies should also evaluate the application of phage therapy in the fish aquarium to prevent and control *M. marinum* infection.

PROBIOTIC STRAINS WITH HYPOCHOLESTEROLEMIC ACTIVITY AS POTENTIAL BASIS OF FOOD SUPPLEMENT FOR PREVENTION AND CONCOMITANT TREATMENT OF CARDIOVASCULAR DISEASES ASSOCIATED WITH HIGH CHOLESTEROL LEVEL

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Globally, about 17 million people die from cardiovascular disease (CVD) every year, accounting for 31% of all deaths worldwide. High serum cholesterol is regarded by many as the main cause of coronary atherosclerosis, and it has been well established that elevated cholesterol is associated with an increased risk of CVD. Apart from modulating the gut functionality, probiotics have also been associated with various other health benefits such as brain functioning, boosting immunity, reducing cholesterol, and promoting metabolic homeostasis through their biological mechanisms in the body.

Several mechanisms of involvement of the microbiome in maintaining lipid metabolism at a physiological level and preventing the development of hypercholesterolemia are assumed: deconjugation of bile acids and reduction of their resorption due to the synthesis of specialized hydrolases; incorporation of cholesterol into the lipid layer of the cell membrane; transformation of cholesterol into coprostanol and its removal from the body together with feces; inhibition of cholesterol synthesis in the liver.