Innovative products for replacing antibiotics : A milestone from research to business

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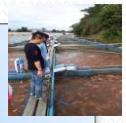
Outline

- Innovative products for replacing antibiotics : A milestone from research to business
- AMR and AMU in Aquaculture
- The methods for reducing AMR and replace antibiotics.
- Non-antibiotic approaches for combat tilpia bacterial pathogens
- Summary

Innovative products for replacing antibiotics : A milestone from research to business

Bacterial diseases outbreak of fish farms



Standard bacterial identification, characterization,antimicrobial susceptibility, and genome analysis

List of solutions for replacing antibiotics use :

-Vaccines

-Probiotics, Postbiotics

-Immunostimulants

-Bacteriophage cocktails

-Herbs

- Supplements

Design researcher and student team members for each solutions

Products prototype testing :

-Laboratory testing

- On farm testing

Up-scale production, PR and Marketing

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OUR MISSON

The Center of Excellence in Fish Infectious Diseases (CE FID) in cooperation with Faculty of Veterinary Science, Chulalongkorn University makes an effort to improve sustainable aquaculture . We aim to perform research in fish disease prevention and control as well as provide disease diagnosis services to fish farmers in order to minimize impact of serious diseases of fish farming .

RESEARCH & ACTIVITIES

- Diseases surveillance and diagnosis
- Develop vaccines , innovative products or strategies to prevent diseases
- Encourage graduate students and researchers in aquatic health science
- Provide training courses and workshops to veterinarians and scientists in aquaculture field
- Provide fish health inspectorate and disease diagnosis to fish farms

Fish Infectious Diseases CE

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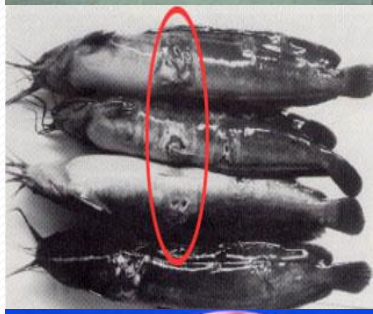
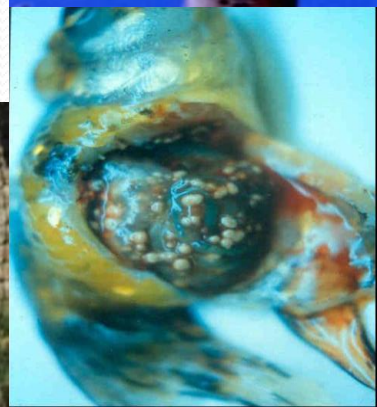
Chula Chulalongkorn University

Bacterial Diseases in Aquaculture

The sustainable development of the aquaculture sector is hampered by bacterial disease epidemics such as :

- Bacterial hemorrhagic septicemia by *Aeromonas* spp., *Psuedomonas* spp., *Edwardsiella* spp.
- Furunculosis, Ulcerative disease
- Vibriosis
- Enteric septicemia of catfish
- Enteric red mouth disease
- Streptococcosis
- Columnaris disease or Saddleback disease
- Bacterial Kidney Disease (BKD)
- Tuberculosis, Mycobacteriosis
- Nocardiosis
- Piscicricketsiosis
- Franciscellosis
- Photobacteriosis

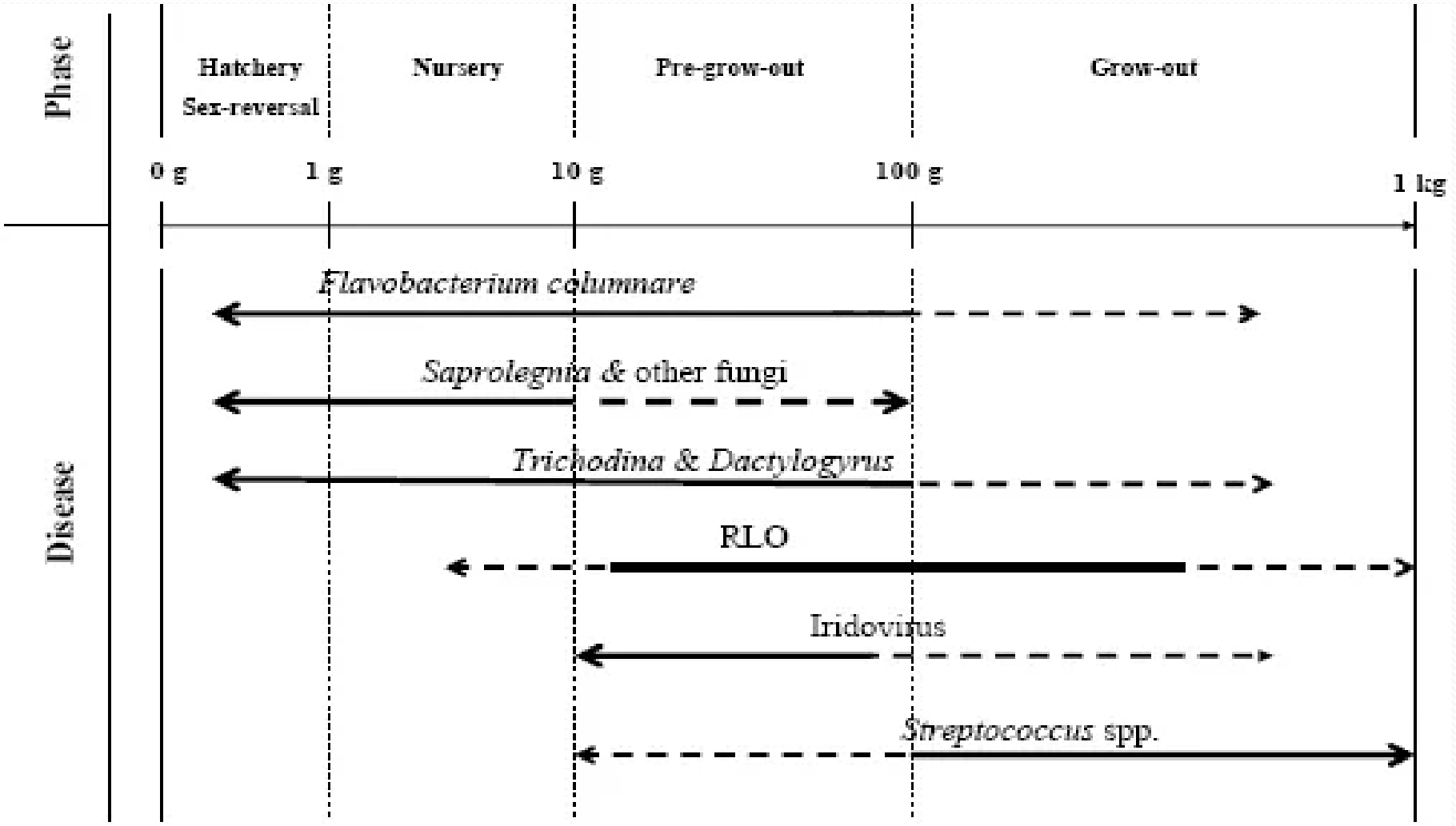




Important bacterial diseases of Tilapia

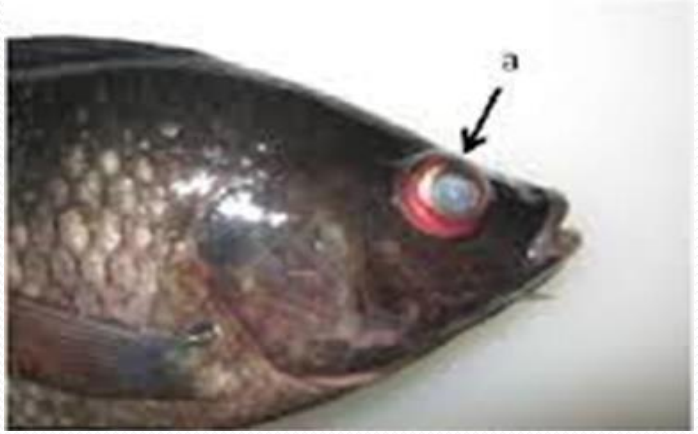
- Streptococcosis
- Columnaris
- Haemorrhagic septicemia such as Aeromonas septicemia and Edwardsiella septicemia
- Franciscellosis
- Mixed infection or concurrent infections

Tilapia major diseases



Source : http://www.thefishsite.com/articles/139/ diseases-of-tilapia-an-introduction

Streptococcosis

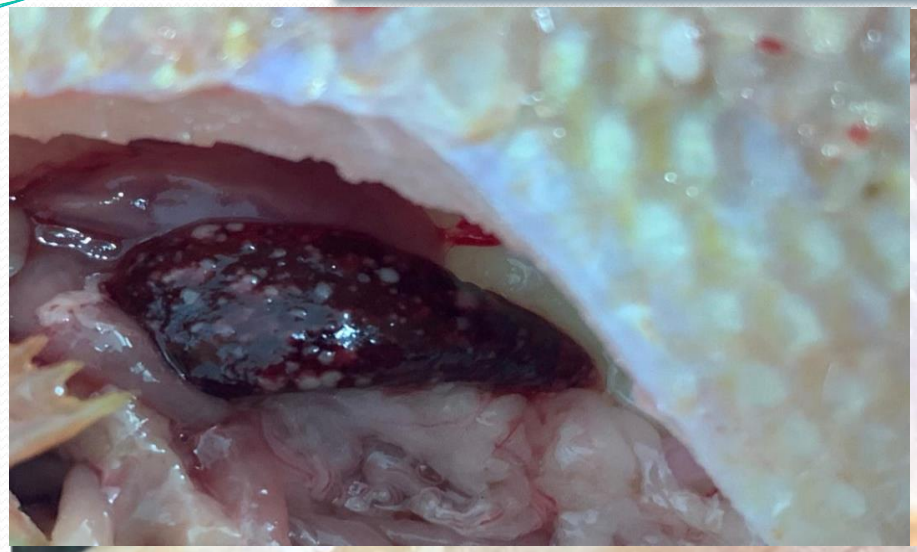


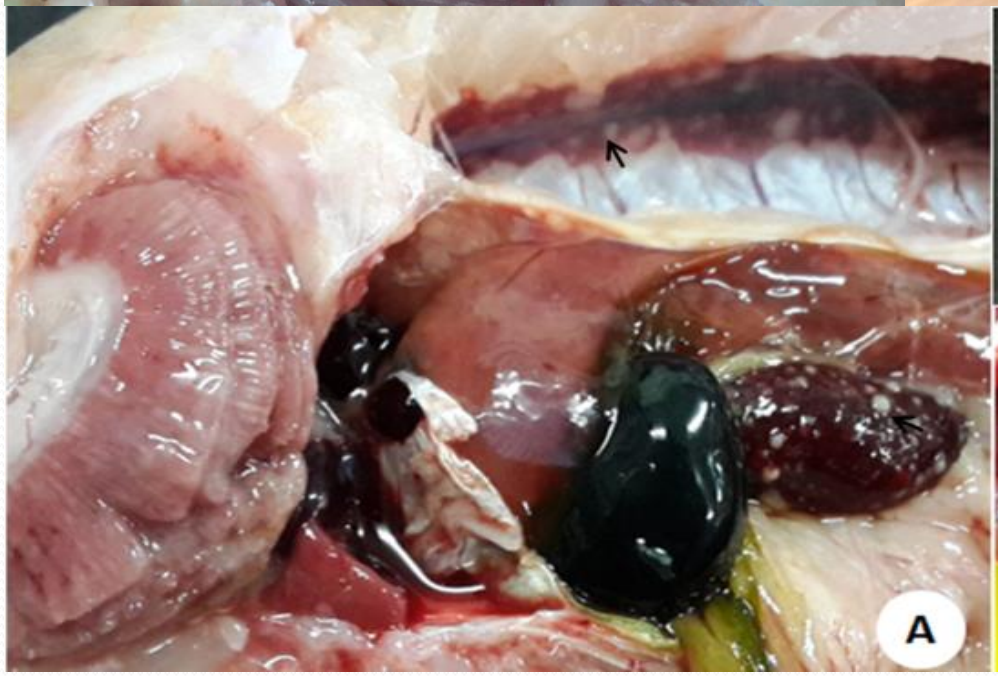
Columnaris disease

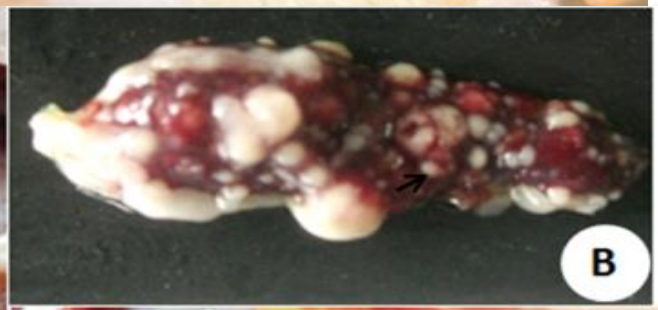
Nile Tilapia *(Oreochromis sp.)*

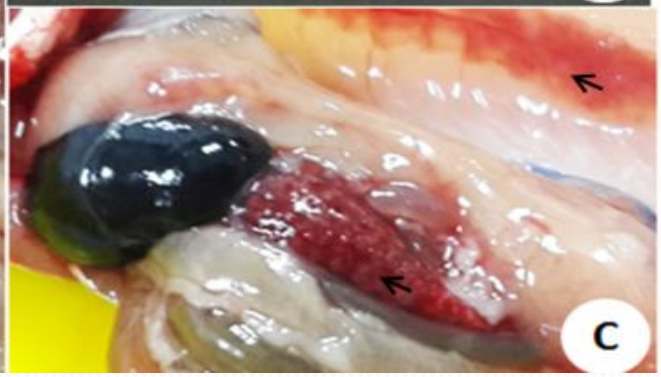
Bacterial hemorrhagic septicemia

Franciscellosis









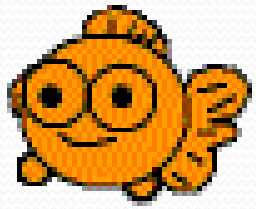
Indications of use and formulations of antimicrobials used in Aquaculture

- treatment of Major bacterial infections : *Aeromonas* spp, *Vibrio* spp., *Streptococcus* spp.
- Licensed use in generalized conditions (septicemia), skin ulcers
- Formulations : oral (feed medication), water bath

List of licensed antimicrobials used in aquaculture

- Amoxycillin
- Enrofloxcin
- Sarafloxacin
- Oxolinic acid
- Oxytetracycline
- Sulfadimethoxine sodium / Ormethoprim
- Sulfadimethoxine sodium / Trimethoprim
- Sulfadiazine and Trimethoprim
- Sulfadimidine and Trimetroprim
- Sulfamonomethoxine Sodium
- Toltrazuril

Quinolone licensed for use in fish by region of the world



- Enrofloxcin (Asia)
- Sarafloxacin (Europe)
- Flumequine (Asia)
- Oxolinic acid (Japan, Latin America)

Quinolones was no licensed in USA, Canada, Australia and South Africa

Data complied from WHO/EMC/ZDI/98.10

Problems of non-prudent use of antimicrobials in Aquaculture

- Antibiotic resistance
  - in animals
  - in human
  - in environment
- Antibiotics residue
  - Drugs allergy
  - Carcinogenesis

The risk on public health of the use of antimicrobials in aquaculture

1. Antimicrobial resistance (AMR) :

- The use of antimicrobial agents can lead to the emergence of antimicrobial resistant microorganisms and further promote the dissemination of resistant bacteria and resistance genes (OIE/FAO/WHO 2004a).
- The use of antimicrobials in aquaculture can have an impact on the resistance situation in another area, such as in human medicine, and resistance problems in one country can spread to another country.

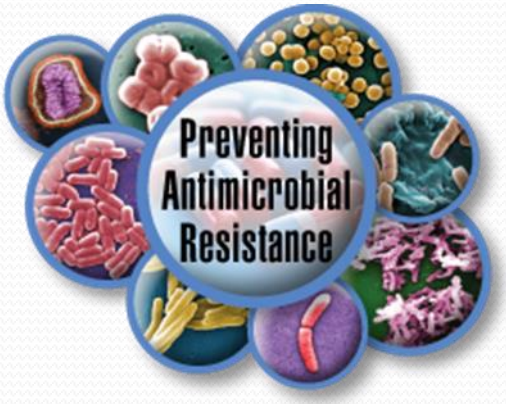
2. Antimicrobial residues :

- Antimicrobial usage in aquaculture can result in residues of antimicrobials in the food products and environments.

Antimicrobial resistance often found in Aquaculture

- Quinolone and fluoroquinolone resistance

- Chloramphenicol resistance
- Tetracycline resistance



- Beta-lactam resistance
- Multi-drugs resistance (MDR)

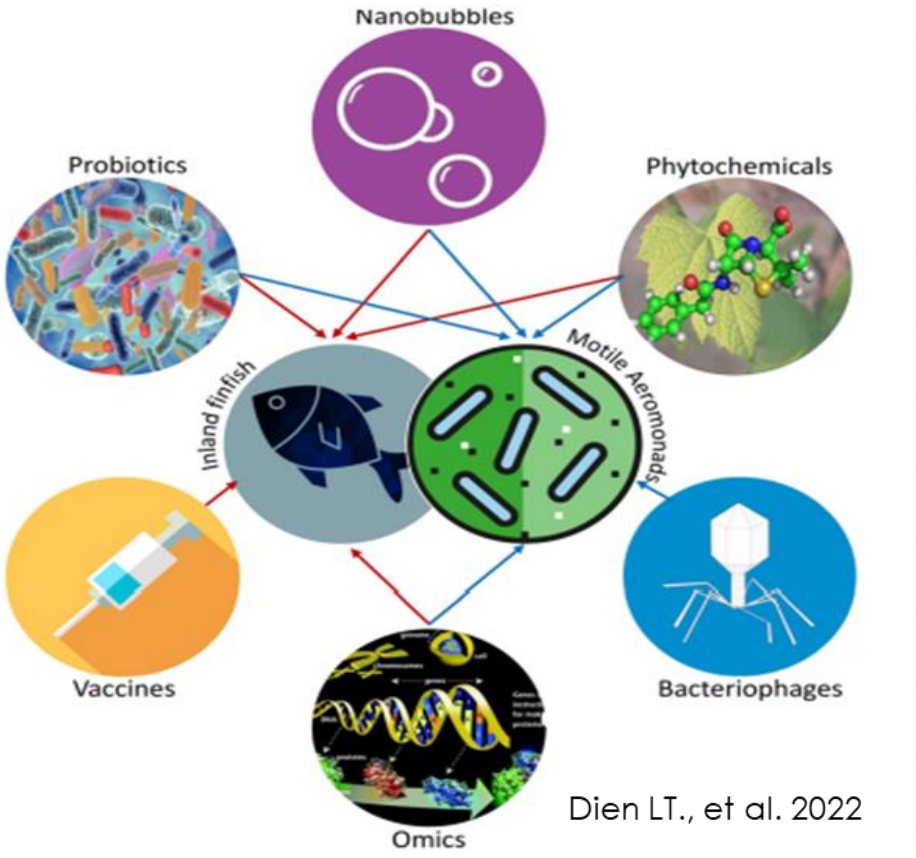
The methods for reducing AMR in aquaculture

- Promoting biosecurity, water quality management, and improving broodstock, and fingerling quality.
- Prudent use of antimicrobials in aquaculture
- Non-antibiotics approaches or Alternative To Antibiotics (ATAs) in aquaculture :

ATAs are any substance or management strategy that can be substituted for antibiotics that are increasingly becoming ineffective against pathogenic bacteria due to AMR.

Non-antibiotics approaches or Alternative to Antibiotics (ATAs) for combat bacterial diseases in aquaculture

- Vaccines
- Immunostimulants
- Phytobiotics
- Probiotics and Synbiotics
- Bacteriophages
- Nanobubble
- etc.



Vaccines

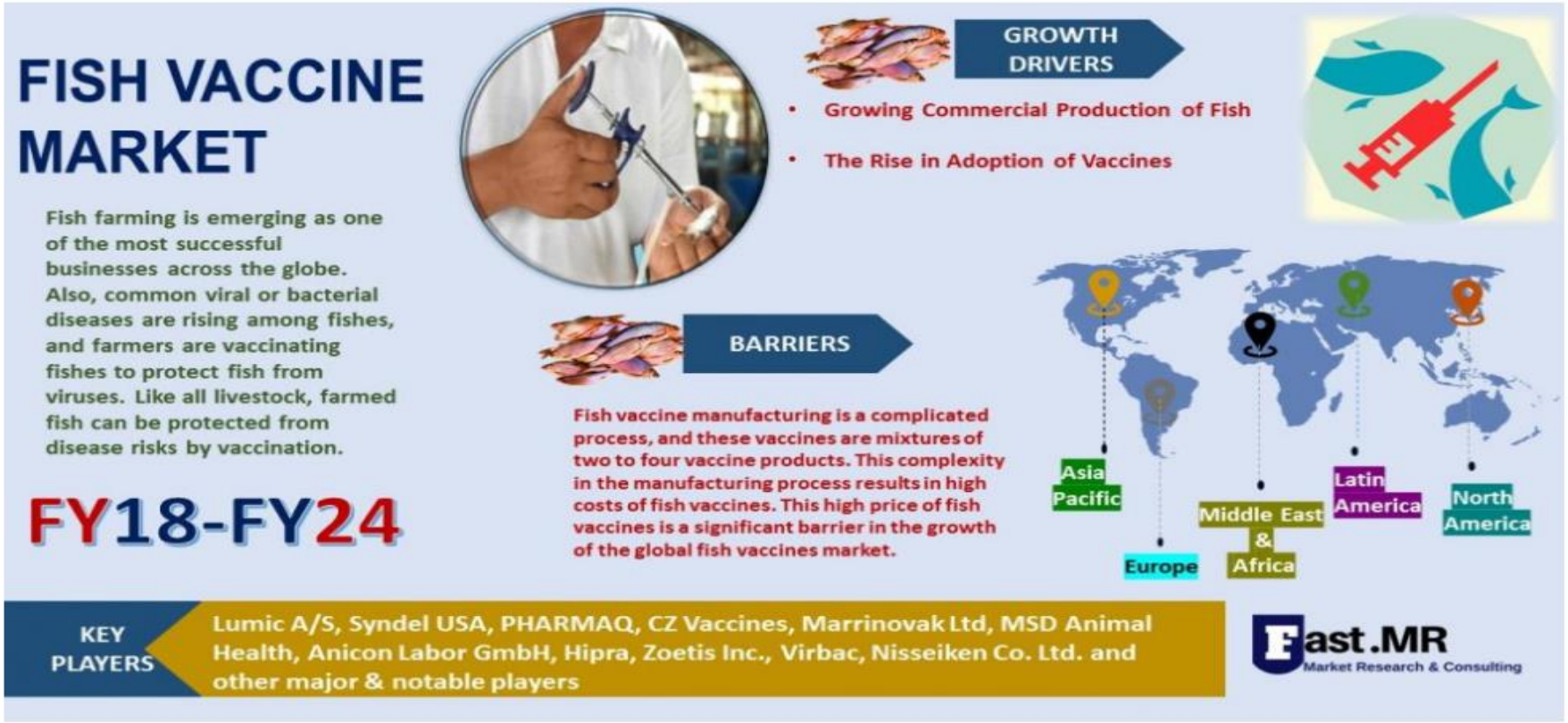
- Up to now, many vaccines for tilapia have been developed and experimentally tested.
- It is hard to compare the results of these studies due to the differences in fish species and breeds, vaccine preparations (e.g., immunization dose, type of vaccine, adjuvant), immunization and challenge methods, and the duration of vaccination trials.
- Standard experimental design and guidelines for specific fish species and other general regulations issued by authorities within each country should be established.
- Future vaccines should be in the form of multivalent vaccines, efficient and affordable for small fish farmers.

Dien LT., et al. 2022

NEWS

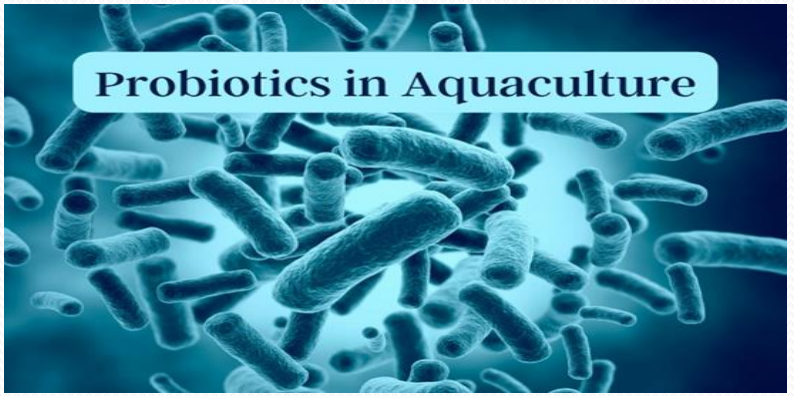
Fish vaccine Market – Industry Analysis, Size, Share, Growth, Trends and Forecast 2018 – 2024

December 2, 2019 7 Min Read



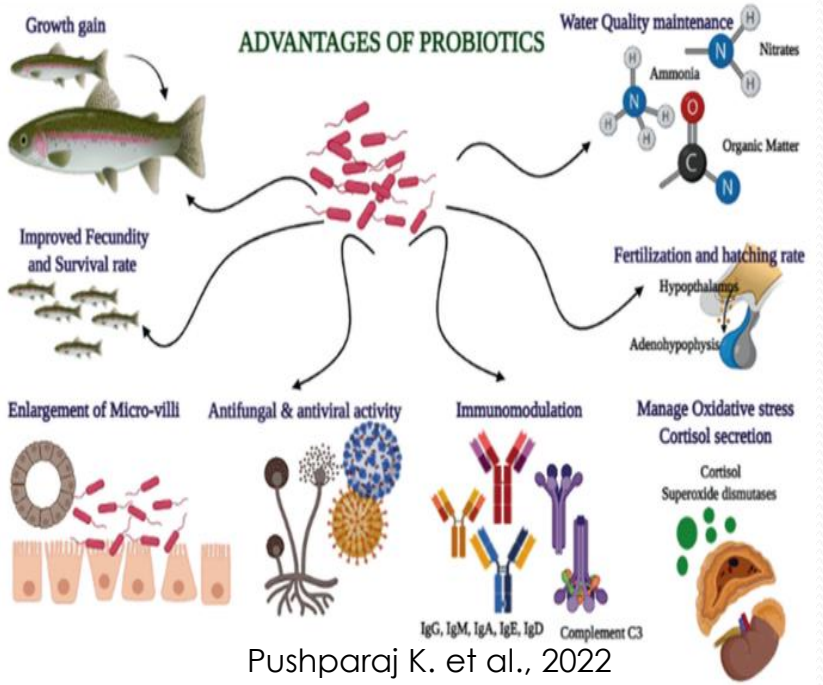
https://hitzdairies.com/2019/12/02/fish-vaccine-market-industry-analysis-size-share-growth-trends-and-forecast-2018-2024/

Probiotics and Synbiotics-based approach (1)



The effects of probiotics include :

- activating the immune defense
- improving intestinal microbial balance
- improve growth performance and survival rate of the host
- Competitive with the pathogens
- production of inhibitory substances or interference of quorum sensing of pathogenic bacteria
- maintaining water quality and controlling phytoplankton
- enhancing physiological processes and reproductive performance of aquatic organisms



Pushparaj K. et al., 2022

Dien LT., et al. 2022

Probiotics and Synbiotics-based approach (2)

- probiotic-based products : including synbiotics (probiotics–prebiotics) and tri-biotics (probiotics–prebiotics–postbiotics) need to be investigated on a laboratory scale and industrial scale to optimize feed formulation for aquatic animals.

- The encapsulation technology should be applied to avoid a large fluctuation in the quality of probiotics.

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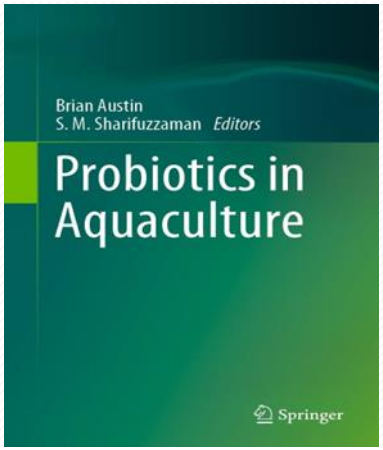

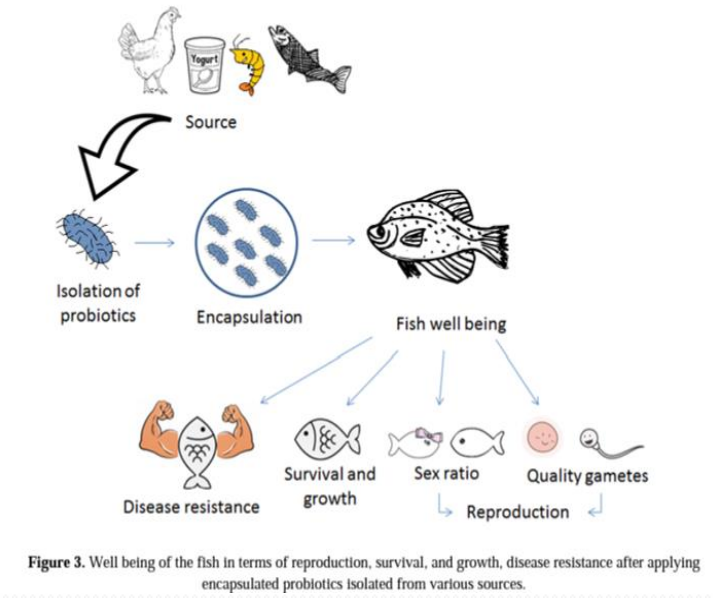

Figure 3. Well being of the fish in terms of reproduction, survival, and growth, disease resistance after applying encapsulated probiotics isolated from various sources.

Ishthiaq IB., et el. 2021

Phytobiotics-based approach (1)

- Phytogenics, phytochemicals or phytomedicines are natural bioactive compounds extracted from numerous kinds of plants.
- They are ecofriendly and safe for humans and animals, including aquatic organisms.
- Based on their synthetic pathway, phytogenics can be divided into three major groups: terpenoids, phenolic metabolites and alkaloids, and other nitrogen-containing metabolites.
- Phytochemicals can be extracted from many parts of fresh or dried plants such as roots, leaves, barks, flowers, fruits and seeds.

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Phytobiotics-based approach (2)

Suggestions for further investigation :

- discover novel phytochemical plants, and novel combinations between plant-based and probiotic-based products

- optimize the extraction process and standardize feed formulation, dose, and duration

- increase of long-term stability and enhancement of bioavailability of phytomedicines using encapsulation technology and nanotechnology

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Bacteriophages-based approach

- Phages can be used as therapeutic or prophylactic agents based on the type of infection and target organisms.
- The narrow host range and phage-resistant bacteria are two significant challenges in the widespread use of phages in aquaculture.
- The barrier to phage therapy in aquaculture is related to the transfer of bacterial antibiotic resistance genes or virulence genes.

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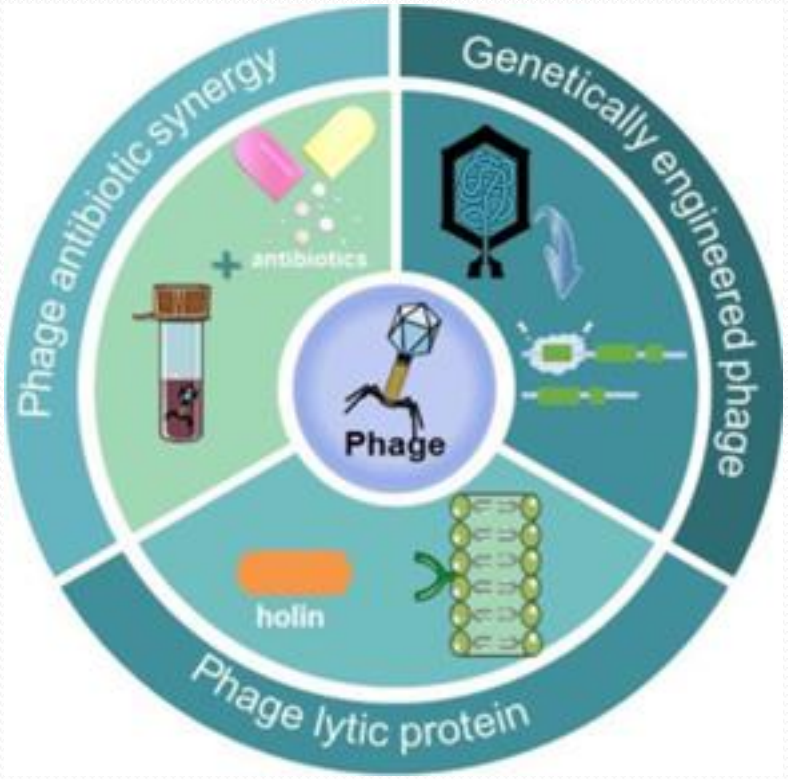
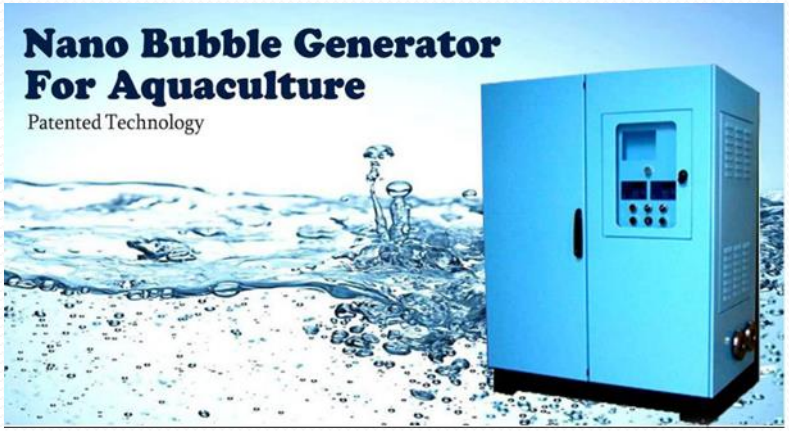


Liu R. et al., 2022

Nanobubble based-approach (1)

- Nanobubbles are bubbles with a diameter <200 nm and have neutral buoyancy that enables them to have a long residence time in solution.
- They are generated commonly by decompression and gas–water circulation-type generators.
- Nanobubble technology has been applied in wastewater treatment, flotation, surface cleaning, and defouling.



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Nanobubble based-approach (2)

- In aquaculture, nanobubbles are considered an emerging technology for water treatment.
- Oxygen nanobubbles can increase DO in the aquaculture systems resulting in improved growth performance of fish and shrimp.
- Ozone nanobubble is a powerful disinfectant to reduce pathogen concentration and improve water quality in both flow-through and recirculating aquaculture systems.

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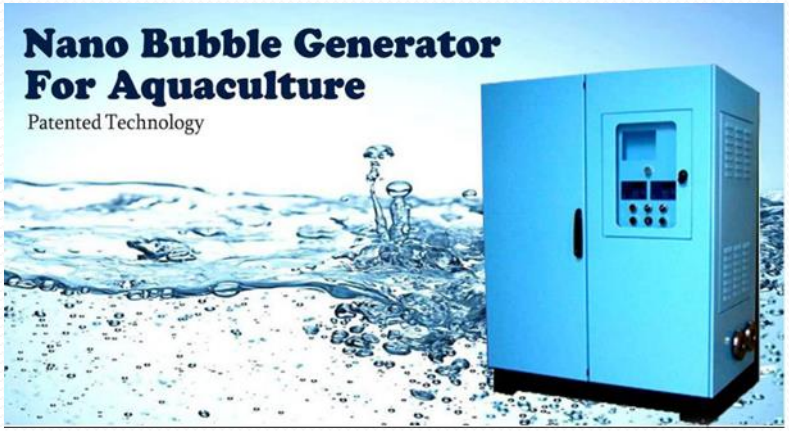


Summary (1)

- rapid increase in therapeutic and prophylactic usage of antimicrobials in aquaculture including those important in human therapeutics such as fluoroquinolone and beta-lactam antibiotic.

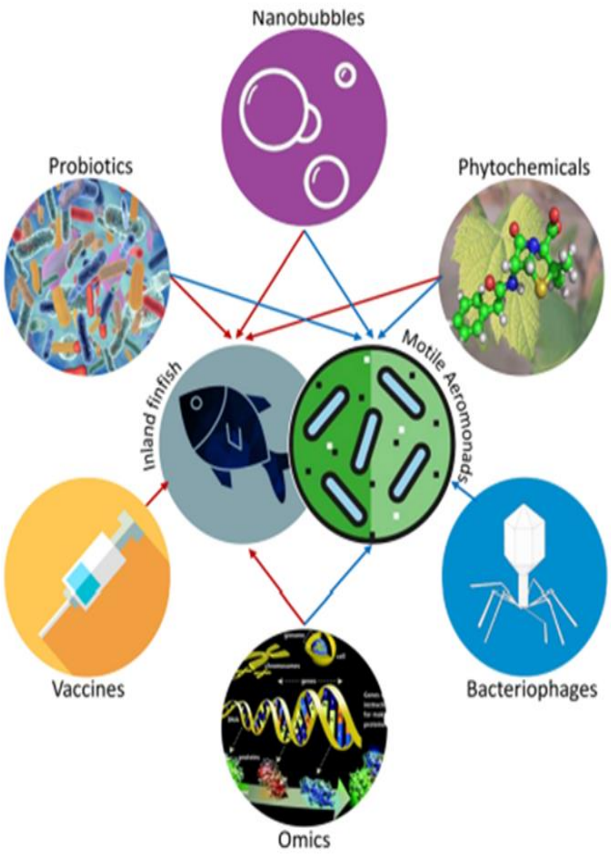
- AMR can be transmitted between human pathogens and animal pathogens.

- Massive use of antimicrobials in aquaculture can negatively impact animal and human health as well as the aquatic environment and should have prevention and control.

Summary (2)

- ATAs can be substituted for therapeutic drugs that are increasingly becoming ineffective due to AMR.

- Non-antibiotic approaches can minimize the need for antibiotics to combat infectious diseases in animal and human health.



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Summary (3)

- In aquaculture, along with promoting biosecurity, water quality management, and improving broodstock, and fingerling quality, ATAs are urgently needed in both prophylactics and therapeutics.

- More research and innovation related to non-antibiotic approaches or ATAs in aquaculture are required.

Thank you for your attention

Antimicrobial resistance : No action today, No cure tomorrow