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Responsible Use of Antimicrobials in Indian Aquaculture

Opportunities and Challenges

7th December, 2016

ICAR - CIBA, Chennai

Organised under

ALL INDIA NETWORK PROJECT ON FISH HEALTH

ICAR - Central Institute of Brackishwater Aquaculture
ISO 9001:2008
(Indian Council of Agricultural Research)
75, Santhome High Road, R.A. Puram, Chennai - 600028, Tamil Nadu, India.

FIGHTING ANTIBIOTIC RESISTANCE

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Antibiotics are essential resources for human health, animal health and animal welfare.

We need to collectively ensure the responsible and prudent use of antibiotics in animals to preserve their effectiveness.

WORLD ANTIBIOTIC AWARENESS WEEK

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PROCEEDINGS

Responsible Use of Antimicrobials in Indian Aquaculture

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This brainstorming workshop on "Responsible Use of Antimicrobials in Indian Aquaculture: Opportunities and Challenges" on 7th December 2016 is being conducted at ICAR-CIBA as part of call for "World Antibiotic Awareness Week" during 14-18th Nov 2016 jointly given by World Organization for Animal Health (OIE), Food and Agriculture Organization (FAO) and World Health Organization (WHO).

#AntibioticResistance

WORLD ANTIBIOTIC AWARENESS WEEK

14-20 NOVEMBER 2016

HANDLE ANTIBIOTICS WITH CARE

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Editorial Committee	Dr. Prassana Kumar Patil Dr. S. V. Alavandi Dr. S.K. Otta Dr. Satheesha Avunje Dr. R. Ananda Raja

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TOPICS OF DISCUSSION

- **Classification of antibiotics used in food production**

  K. Ashok Kumar, T. V. Sankar, ICAR - Central Institute of Fisheries Technology, Kochi, Kerala

- **Pharmacokinetics and pharmacodynamics of antibiotics in aquatic animals**

  Satheesha Avunje and P.K.Patil Aquatic Animal Health and Environment Division, ICAR - CIBA, Chennai

- **Molecular mechanisms of antimicrobial resistance**

  Subhendu Kumar Otta and P.K.Patil Aquatic Animal Health and Environment Division, ICAR - CIBA, Chennai

- **Antibiotic Use in Health Care Systems: Regulations and Practices**

  Sujith J Chandy, Christian Medical College, Vellore, Tamil Nadu.

- **Role of non-human use of antibiotics in development of resistance in bacterial pathogens of public health importance.**

  Padma Krishnan, Institute of Basic Medical Sciences, University of Madras, Chennai.

- **Antibiotic usage patterns in animal husbandry and food safety: Regulations and practice.**

  S.Ramesh, Tamil Nadu Veterinary and Animal Sciences University (TANUVAS), Chennai.

- **Antibiotic usage patterns in agriculture and food safety: Regulations and practice.**

  V.Paranidharan, Tamil Nadu Agriculture University, Coimbatore, Tamil Nadu.

- **Antibiotic usage patterns in sericulture for productivity enhancement**

  R.N. Bhaskar and H.G. Anusha, University of Agricultural Sciences (UAS), Bengaluru

- **Challenges in regulating use of antimicrobial agents in Indian aquaculture**

  P.K.Patil and Satheesha Avunje, K.K. Vijayan, Aquatic Animal Health and Environment Division, ICAR - CIBA, Chennai

- **Determination of antibiotic residues in fish/meat**

  T. V. Sankar, K. Ashok Kumar, Central Institute of Fisheries Technology, Kochi, Kerala

- **Fate of antibiotics in environment**

  Kumararaja, R.Saraswathi, P.K.Patil, N. Lalitha and M.Muralidhar, Aquatic Animal Health and Environment Division, ICAR-CIBA, Chennai

- **Indian shrimp trade in International markets with respect to antibiotics and other Sanitary and Phyto Sanitary (SPS) measures**

  T. Ravisankar, Social Science Division, ICAR-CIBA, Chennai

- **Alternatives to antibiotics in aquaculture**

  R. Ananda Raja, S. K. Otta and S.V. Alavandi, Aquatic Animal Health and Environment Division, ICAR-CIBA, Chennai

- **Biodynamic preparations is an alternative for antibiotics in food production**

  M. Sakthivel, Hatsun Agro Products Limited, Chennai

PROGRAMME SCHEDULE

7th December, 2016

10.00 to 10.30	**PROGRAMME INAUGURATION**
Welcome address	**Dr. S. V. Alavandi** *Principal Scientist and Head* *Aquatic Animal Health and Environment Division (AAHED)* *ICAR-CIBA, Chennai*
Background information of the workshop	**Dr. P. K. Patil** *Senior Scientist and Project Coordinator (AINP-FH)* *Aquatic Animal Health and Environment Division (AAHED)* *ICAR-CIBA Chennai*
Inaugural address	**Dr. K. K. Vijayan** *Director and National Coordinator (AINP-FH), ICAR-CIBA Chennai*
Vote of thanks	**Dr. S.K. Otta** *Senior Scientist, Aquatic Animal Health and Environment Division (AAHED), ICAR - CIBA Chennai*

10.30 - 01.30 TECHNICAL SESSION-I

10.30 - 11.00	**Antibiotic Use in Health Care Systems : Regulations and practices** **Dr. Sujith J Chandy,** *Professor, Clinical Pharmacology, Christian Medical College, Vellore, Tamil Nadu*
11.00 - 11.30	**Role of non-human use of antibiotics in development of resistance in bacterial pathogens of public health importance** **Dr. Padma Krishnan,** *Assistant Professor, Dept. Microbiology, Dr. ALM PGIBMS, University of Madras, Chennai*
11.30 - 12.00	**Antibiotic usage patterns in animal husbandry and food safety: Regulations and practices** **Dr. S. Ramesh,** *Professor and Head, Laboratory Animal Medicine, Tamil Nadu Veterinary and Animal Sciences University (TANUVAS), Chennai*
12.00 - 12.30	**Antibiotic usage patterns in agriculture and food safety: Regulations and practices** **Dr. V. Paranidharan,** *Professor (Plant Pathology), Tamil Nadu Agriculture University, Coimbatore, Tamil Nadu.*

12.30 - 01.00	**Antibiotic usage patterns in sericulture: regulations and practice** **Dr. R.N. Bhaskar,** *Professor (Sericulture), University of Agricultural Sciences (UAS), Bangaluru*
01.00 - 01.30	**Antibiotics in aquaculture regulations worldwide and challenges in India** **Dr. P.K. Patil,** *Senior Scientist, Aquatic Animal Health and Environment Division (AAHED), ICAR-CIBA, Chennai*
01.30 - 2.00	**Lunch Break**
2.00 - 5.00 TECHNICAL SESSION II	
2.00 - 2.30	**Drugs and chemicals used in Indian aquaculture** **Dr. M. Muralidhar,** *Principal Scientist, Aquatic Animal Health and Environment Division (AAHED), ICAR-CIBA Chennai*
2.30 - 3.00	**Biosafety evaluation of the drugs in aquatic animals** **Dr. Satheesha Avunje,** *Scientist, Aquatic Animal Health and Environment Division (AAHED), ICAR-CIBA Chennai*
3.00 - 3.30	**Pharmacokinetics and pharmacodynamics of drugs in aquatic animals** **Dr. P.K. Patil,** *Senior Scientist, Aquatic Animal Health and Environment Division (AAHED), ICAR-CIBA Chennai*
3.30 - 4.00	**Evaluating disinfectants in aquatic animals** **Dr. S.K. Otta,** *Senior Scientist, Aquatic Animal Health and Environment Division (AAHED), ICAR-CIBA Chennai*
4.00 - 4.30	**Economic loss assessment of aquatic animal diseases** **Dr. T. Ravisankar,** *Principal Scientist, Social Sciences Division (SSD), ICAR-CIBA, Chennai*
4.30 - 5.00	Concluding remarks and valedictory function

Responsible Use of Antimicrobials in Indian Aquaculture

Opportunities and Challenges

BACKGROUND FOR THE WORKSHOP

P.K. Patil

Aquatic Animal Health and Environment Division, ICAR-CIBA, Chennai

Antibiotics one of the land mark discoveries of humanity are being used for the last 85 years for controlling bacterial infections in human medicine, animal husbandry and agriculture. Considering their growth promoting properties, use of these substances has increased substantially in food animal production sector. In an effort to achieve better control of infections in human healthcare and enhance the productivity in food animals, antibiotics are being used indiscriminately both in developed and developing countries. This mishandling has led to the development of resistance against these substances in pathogenic and environmental microbes in addition to the build-up of their residues in nature leading to environmental toxicity. Further, these residues may affect the natural population of micro fauna that have pivotal role in maintaining the environmental balance. Since the antibiotics are the essential requirements for healthcare systems and food production, it is imperative that they should be used responsibly both in medicine and agriculture. Bacteria acquire resistance against antibiotics quicker than development of new antibiotic itself and unfortunately no new class of antibiotics have been developed since four decades. Hence it is essential that concerted effort should be made to preserve the effectiveness of available antibiotics to ensure human health and sustained food production.

Use of antibiotics in food animal production sector in India

Antibiotics are used regularly as growth promoters in organized dairy, beef, poultry and swine production in developed world. Such non-therapeutic use in feedlots has been indicated as major cause of antibiotic resistance development. Similar analogy is also drawn for antibiotic use in animal food production systems of developing and underdeveloped countries. In countries like India where dairy is a livelihood option supporting the agricultural income and piggery is a backyard activity. Both these sectors doses not practice growth promotion using antibiotic. Additionally the beef industry is non-existent and swine industry is in its infancy, farming done in few north eastern states of the country. Prophylactic use of antibiotics in poultry industry is definitely a cause of concern and needs to be addressed. Similarly prophylactic and metaphylactic use of antibiotics in aquaculture in super and high intensive fish farming requires attention. More than half of Indian fish production is still from capture fisheries and aquaculture is dominated by low input freshwater carp farming and semi-intensive brackishwater shrimp farming. The use of antibiotics as growth promoter in freshwater aquaculture is not economically viable and the same is not practiced in shrimp farming due to international trade restrictions. It is interesting to know that economically important disease of fishes are mainly parasitic infestations and in shrimp farming, viral diseases are main causes. Either of the case does not warrant the application of antibiotics.

Fate of antibiotics in nature

Manure from livestock including poultry is considered one of the important sources of antibiotic residue build-up in the natural environments as they are directly applied to agricultural fields and traditional aquaculture ponds to enhance natural productivity. Fate of antibiotics in receiving environment and persistence of residues for longer periods in the nature is one of the key issues debated worldwide. Rate of antibiotic degradation depends almost entirely on photo period and environmental temperature and hence the degradation of antibiotics in environments in tropical countries including India is expected to be faster by many orders compared to temperate regions. There is a lack of scientific data on photolysis, hydrolysis and microbial degradation of antibiotics in warmer countries. This has resulted in relying on the data generated in temperate regions and generalizing the information. Therefore there is an urgent need to generate such information so that suitable strategies may be developed for reduction of environmental toxicity of antibiotics used in food producing animals.

Antimicrobial resistance in nature

Several studies worldwide have reported the isolation of multi-drug resistant microbes form the natural water bodies and suggest that the agricultural use of antibiotics as main reason for such antimicrobial resistance patterns. In most of the developing countries including India according to one estimate more than 70 percent of the urban sewerage dose not pass through treatment plants suggesting the role of anthropogenic activities in contaminating the natural water bodies with antibiotic residues and antibiotic resistant microbes. Additionally, over the counter sale of antibiotic is a common practice in India which is complicating the process of regulating the medical use of antibiotics.

Information on antibiotic market

Data on use of total production, sale and use of antibiotics in different sectors is available in the developed countries which make it easy to quantify the usage of these substances in different fields and implement the control measures accordingly. However similar data is not available from India. In the absence of such credible data international agencies are using data generated by non-governmental organizations as reference and conclude that the developing countries like India use antibiotics extensively in food animal production. Availability of such information in the digital media unduly damage image of the Indian seafood quality affecting the international trade.

Regulating antibiotics

In most of the developed countries usage of antibiotics in medical and agriculture sectors is regulated by legislations and is implemented strictly. Absence of any such regulations in India for antibiotic usage in aquaculture has led to presumed misuse/abuse/over use of drugs/medicines creating the doubts in the minds of domestic and international consumers of animal food. Hence there is an urgent need to develop such regulations with guidelines for the sector so that the farmers are aware of drugs legally permitted to use and follow the farming practices accordingly.

Alternatives to antibiotics

Several workshops/conferences have suggested to the need for developing and promoting the use of alternate prophylactic measures to reduce the dependence of antibiotics in food animal production. It is interesting to note that in one of our recent surveys on drug/medicine usage patterns in Indian aquaculture revealed more than 70 percent of the medicines used are prophylactic substances including probiotics, immunostimulants and disinfectants and suggested the marginal use of therapeutic agents.

With this background this brainstorming workshop has been organized with experts from major sectors of human, veterinary, crop protection, sericulture and aquaculture sectors to deliberate on the use of antibiotics, contribution to the development of antibiotic resistance microbes and to suggest suitable mitigatory measures. Generation of geographically specific data under Indian conditions would help in better understanding of the issue so that suitable strategies may be developed. Outcome of this meeting would help in focusing our research towards generation of basic data on antibiotic usage pattern, suggest practices for scientific use, establish methodologies for surveillance of antibiotic resistant microbes and residues in foods and the environments, and develop mitigatory measures. Such information would help the nation to develop guidelines required for developing legal provisions for effective and safe use of antibiotics in Indian food production sector.

AQUACULTURE PRODUCTION IN INDIA

K.K. Vijayan, S.V. Alavandi and P.K. Patil

Aquatic Animal Health and Environment Division, ICAR-CIBA, Chennai

Aquaculture has been one of the most important sectors in India for food production, livelihood, employment and revenue generation. Since independence with implementation of several policies and schemes, aquaculture production has observed tremendous growth. India stands second after China in aquaculture production, harvesting 4.88 million metric tonnes and exported 9.8 million metric tonnes earning ₹ 30,213 crore as foreign exchange. With increased disposable income of Indian public, demand for healthy food is increasing. Fish being healthy compared to other animal foods, demand for fishery products has accelerated. Capture fishery has been on static and has lesser opportunity to increase production, hence the demand need to be fulfilled by the culture sector. Furthermore, increase in population creates higher demand for food whereas productivity in agriculture and animal husbandry is reaching saturation; potential of aquaculture needs to be explored. Intervention of modern technology has outpaced aquaculture growth (3.2%) with increase in human population. Average percapita fish consumption in developed countries has increased from 9.9 kg in 1960s to 14.4 kg in 1990s and 19.7 kg in 2013. However, percapita fish consumption in developing and under-developed countries is far below (3.5 to 7.6 kg) than in developed countries. World capture fishery for the year 2014 was 81.54 million metric tonne while from aquaculture was 73.8 million metric tonne and in years to come, aquaculture production is expected to surpass capture fisheries.

Growth of aquaculture in India

Aquaculture is an important economic activity in India which has grown by 11 fold, 0.75 million tonnes in 1950-51 to 9.6 million tons in 2012-13 with an annual growth of 4.5 percent. India farming systems generated an employment for 14.5 million people. Total fish production in India for the year 2014 was 4.88 million tonnes from aquaculture, 3.41 tonnes from marine capture and 1.3 million tonnes from inland capture (FAO, 2016). Total aquaculture production includes 4.48 million tonnes of finfish (including 90,000 tonnes of marine finfish), 20,000 tonnes of mollusc and 0.39 million tonnes of crustaceans. India is the 7th in largest exporter of fish and fishery products with an export earnings of 5.60 billion USD in 2014 compared to 1.41 billion USD in 2004 with an annual growth of 14.8%. Further, aquaculture is seen as the best possible option in India to enhance the income generation to world's largest rural population of 857 million. It is estimated that by 2025 total Indian fish production will be growing by 22.6 percent reaching 11.57 billion tonnes, while during the same period aquaculture is expected to grow by 42.2 percent reaching 6.88 billion tones. In spite of this expected phenomenal growth in their sector, one recent study has suggested that along with Bangladesh, Cambodia, China and Philippines, India is also identified as one of the most vulnerable countries for climate change events associated with aquaculture.

Freshwater aquaculture: India has about 2.36 million ha of ponds and tanks that are suitable for freshwater aquaculture while about 40 percent of this is brought under aquaculture. At the same time productivity has been increased from 600 kg/ha/yr in 1970s to 2900 kg/ha/yr in the recent time by implementation of induced breeding technology and composite carp farming. Species diversification will give a new dimension to the Indian freshwater sector. Reservoirs and floodplain wetlands are other major water bodies that have significant potential to increase Indian aquaculture production. Scientific stocking of advanced fish fingerlings in small (1.14 million ha), medium (0.527 million ha) and large reservoir (1.14 million ha) increased productivity from 49 kg/ha/yr, 12.3 kg/ha/yr and 11.43 kg/ha/yr in the period of 1990-2000 to 190 kg/ha/yr, 105 kg/ha/yr and 46kg/ha/yr respectively during the recent time. Floodplain wetlands constitute 0.54 million ha water area in the country, concentrated mostly in the states of Assam, West Bengal, Bihar and Uttar Pradesh. With fisheries management, productivity has been enhanced from 180-350 kg/ha/yr during 1994-95 to 600-1,000 kg/ha/yr, against potential yield of 1200-1,500 kg/ha/yr. Development of pen and cage based culture can enhance productivity of these water bodies. Cold water aquaculture is in its infancy and efforts are continuously made by various government agencies for developing the culture practices in Himalayan states. Major species being promoted in these areas are rainbow trout, mahseer and common carp. Snow trout, the native fish, is also well sought candidate species. These fishes are not only considered for aquaculture but also considered as good sport fishes. Major hill states involved in Aquaculture are Jammu and Kashmir, Himachal Pradesh, Uttarakhand, Sikkim, Arunachal Pradesh, Nagaland and other North Eastern states. State and central government agencies have established hatcheries in these states for supplying seeds for pond culture and stocking in large waterbodies. Himachal Pradesh and Sikkim are the two prominent states involved in the cold water fisheries and aquaculture.

Brackishwater aquaculture: India has about 1.2 million ha of salt affected land suitable for brackishwater aquaculture, of which only 15 percent area has been used for aquaculture. In addition, India has about 9 million ha of inland saline area which is suitable for aquaculture. Development of fish species such as Asian seabass, milkfish, mullets etc. will give more opportunity for brackishwater fish production. Modernization of traditional shrimp farming accelerated brackishwater farming activities in 1980s. Introduction of specific pathogen free domesticated *Penaeus vannamei* in 2009 strengthened the already weakening shrimp farming sector. Major shrimp producing states like, Andhra Pradesh, Tamil Nadu, Gujarat, Maharashtra and Odisha contributed to the total production of 4,34,558 tonnes of shrimp (2014-15). Indian shrimp exports crossed USD 3 billion for the year 2015-16 and major part of which was contributed by *P. vannamei* from brackishwater aquaculture. This is the high time to provide all the required attention to aquaculture in India and enhance the capabilities of the sector to meet the increasing demand for quality fish protein at affordable price

Mariculture : India being a peninsular state, mariculture has a wider opportunity as a source of high quality protein source, livelihood for poor and an alternative job opportunity for fishermen when marine capture fishery is dwindling. Indian mariculture sector predominantly includes culture of finfishes in ponds and cages, marine ornamentals and bivalves, fattening of crabs and lobsters and cultivation of sea weeds. Cobia and silver pompano are the potential fish species for cage culture. Mussel farming in Kerala coast has provided livelihood to thousands and production has crossed 20,000 tonnes in recent years and is a promising low cost venture for coastal village people.

India being agrarian country for centuries, fisheries comes with a several opportunities to mitigate malnourishment in villages, an alternative entrepreneurship for educated unemployed youth and as a business venture for corporate sector.

CIBA'S INITIATIVES IN PROMOTING THE RESPONSIBLE USE OF DRUGS AND CHEMICALS IN INDIAN AQUACULTURE

K.K. Vijayan

Director and National Coordinator (AINP-FH), ICAR-CIBA Chennai

One of the key issues to be addressed in responsible use of drugs/chemicals both in human health and food production is to develop improved health and production standards so that the need for therapeutics is reduced. In this direction ICAR-CIBA has devised several research programmes to develop improved quality standards in finfish and shellfish production systems.

A national flagship ICAR programme, All India Network Project on Fish Health is being operated since 2015 with ICAR-CIBA, Chennai as lead institute with nine other participating centers covering states with major aquaculture activity. One of the major objectives of the program is to monitor through regular survey, profiling and study of drugs/chemicals usage in the aquaculture covering freshwater, brackish and marine rearing systems. The information generated will be used to develop standards for preparation of legal guidelines for the use of drugs/chemicals in aquaculture.

Two major national network projects, National Surveillance Programme for Aquatic Animal Diseases (NSPAAD) funded by National Fisheries Development Board (NFDB) and Consortia Research Project on Development of Vaccines and Diagnostics (CRP on V&D) are also underway in the institute. Under the NSPAAD, prevalence of different infectious diseases of aquatic animals in brackishwater aquaculture in the country are being monitored while under CRP on V&D, cost effective, sensitive, on farm efficient tools for disease diagnosis and prophylactic measures such as vaccination, probiotics and immune stimulants are being developed. It is a concerted effort with a number of partnering institutions distributed all over India and these efforts are expected to reduce the dependence on therapeutic agents particularly antibiotics in management of diseases in aquaculture.

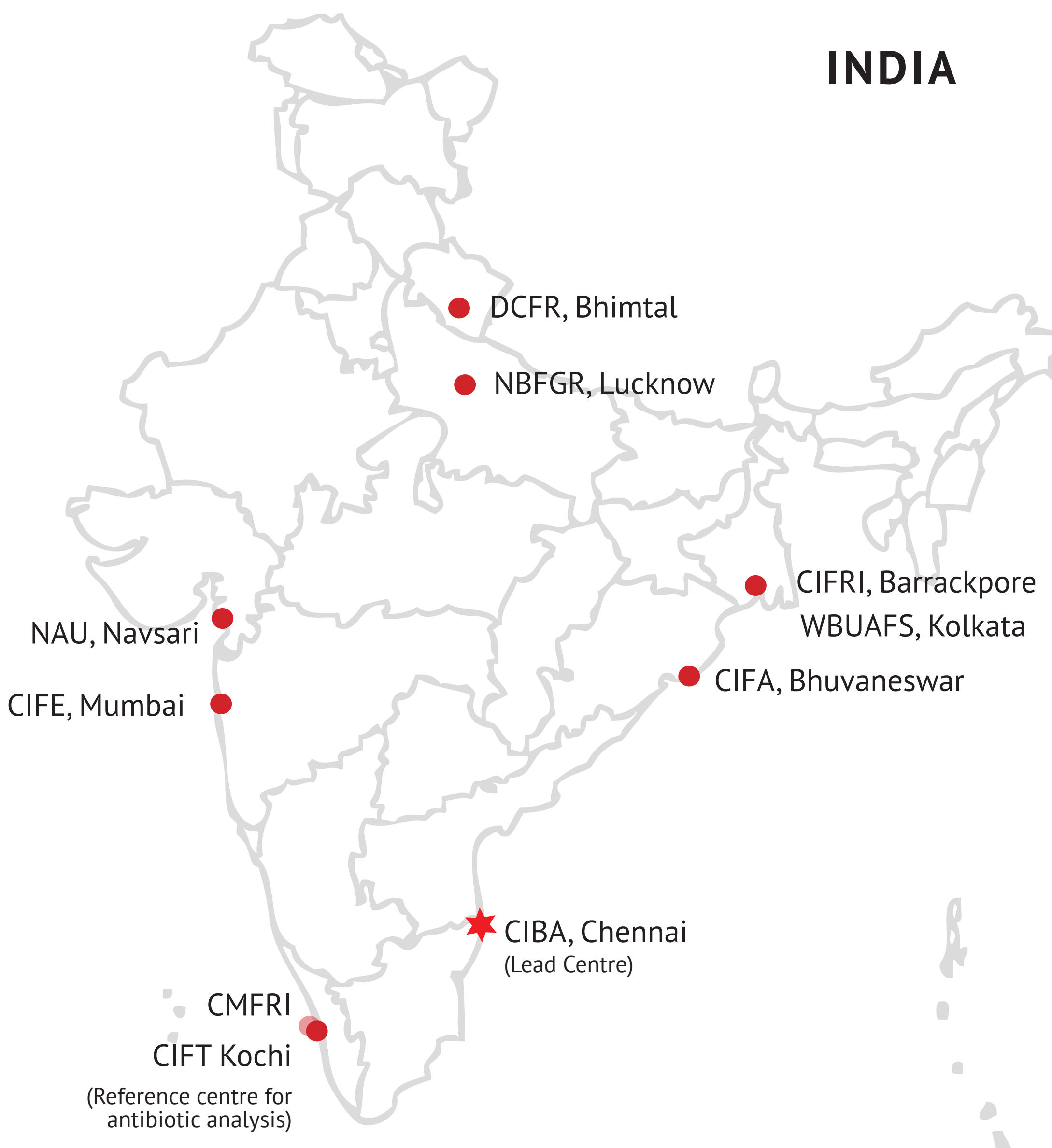
The institute is conducting several research programmes to develop improved Better Management Practices (BMPs) for brackishwater aquaculture, breeding and culture technologies for finfish and shellfish species which are more resistant to diseases with higher productivity. Training programmes are conducted regularly to enhance farmers' awareness on improved BMPs and responsible use of drugs/chemicals in aquaculture. ICAR-CIBA also organize regular training/ harmonization programmes for improving skills and capacities of technical personnel, farm consultants, diagnostic laboratory technicians, hatchery operators and feed manufacturers.

Several collaborative projects with industry partners is being undertaken to address the issues relating the seafood safety and quality. Institute has developed several technologies enhancing the disease management capacities and nutritional quality to achieve improved host and environmental quality and productivity. Institute provides expert technical services to the regulatory agencies such as Coastal Aquaculture Authority (CAA) and Department of Animal Husbandry Dairying and Fisheries (DADF) in developing guidelines for national aquaculture policies.

These research activities ICAR-CIBA is committed to promote responsible use of drugs and chemicals in Indian aquaculture systems to attain socially responsible, environmentally sustainable and economically viable fish farming.

ALL INDIA NETWORK PROJECT ON FISH HEALTH

LEAD CENTER CIBA, CHENNAI



PROJECT TEAM

Lead Institute

ICAR-Central Institute of Brackishwater Aquaculture (CIBA), Chennai

National Coordinator	:	*Dr. K.K. Vijayan, Director, ICAR-CIBA, Chennai*
Project coordinator	:	*Dr. P.K.Patil, Senior Scientist, ICAR-CIBA, Chennai*
Principal Investigator	:	*Dr. P.K. Patil*
Co-Principal Investigators	:	*Dr. S.V. Alavandi, Dr. K.P. Jithendran, Dr. T. Ravisankar, Dr.M. Muralidhar, Dr. R. Saraswathi, Dr. M. Makesh, Dr. S.K.Otta, Mr. Ashok Kumar Jangam, Dr. Sanjoy Das, Dr. R.Ananda Raja, Dr. Kumaraja, Dr. T. Bhuvaneswari, Dr. N. Lalitha, Dr. B. Sivamani and Dr. Satheesha Avunje*

Partner Institutes

ICAR-Central Institute of Freshwater Aquaculture (CIFA), Bhbhaneswar

Principal Investigator	:	*Dr. Priyabrat Swain*
Co-Principal Investigators	:	*Dr. S.S. Mishra and Dr. Rakesh Das*

ICAR-Central Institute of Fisheries Education (CIFE), Mumbai

Principal Investigator	:	*Dr. K. Pani Prasad*

ICAR-Central Marine Fisheries Research Institute (CMFRI), Kochi

Principal Investigator	:	*Dr. N.K.Sanil*
Co-Principal Investigators	:	*Dr. Krupesha Sharma, Dr. P. Shinoj and Dr. M.A. Pradeep*

ICAR-Central Inland Fisheries Research Institute (CIFRI), Barrakpore

Principal Investigator	:	*Dr. S.K. Manna*
Co-Principal Investigators	:	*Ms. Anjana Ekka, Dr. Asit Bera, Dr. Subir K. Nag, Mr. Raju Baitha, Mrs. Preetha Panikkar and Dr. Dipesh Debnath,*

ICAR-Central Institute of Fisheries Technology (CIFT), Kochi

Principal Investigator	:	*Dr. T.V. Sankar*
Co-Principal Investigators	:	*Dr. K. Ashok Kumar*

ICAR-National Bureau of Fish Genetic Resources, Lucknow

Principal Investigator	:	*Dr. P.K. Pradhan*
Co-Principal Investigators	:	*Mr. Chandra Bhushan Kumar and Mr. Aditya Kumar*

ICAR-Directorate on Coldwater Fisheries Research (DCFR), Bhimtal

Principal Investigator	:	*Mr. Sumanta K Mallik*
Co-Principal Investigators	:	*Dr Neetu Shahi and Mr. Ritesh Tandel Shantilala*

West Bengal University of Animal and Fisheries Sciences (WBUAFS), Kolkata

Principal Investigator	:	*Prof. T. J. Abraham*
Co-Principal Investigators	:	*Dr. G. Dash and Dr. T.S. Nagesh*

Navsari Agriculture University (NAU), Navsari, Gujarat

Principal Investigator	:	*Mr. H. G. Solanki*
Co-Principal Investigators	:	*Dr. R. Borichangar, Mr. G.J. Vanza*

ALL INDIA NETWORK PROJECT ON FISH HEALTH
PROJECT PROFILE

Aquaculture is the fastest growing food production sector in India. To sustain this momentum of growth in long run there is an urgent need to develop an effective better management practice (BMPs) to maintain health of host, both in hatchery and grow out culture operations. Intensification in aquaculture has deteriorated the culture environment and increased susceptibility of the host to opportunistic pathogens leading to economic loss due to growth retardation and mortality. Though implementation of BMPs are sufficient to manage the culture intensification use of drugs has been a necessity in recent times. Several drugs/medicines/chemicals are being used to manage the culture systems worldwide.

Many of the countries involved in aquaculture activity have established mechanism for approval of veterinary drugs in aquaculture. Centre for Veterinary Medicine (CVM) under USFDA conducts Aquatic Animal Drug Approval Partnership Programme (AADAP) to ensure safe and effective drugs/medicines for use in aquaculture. The European Medicines Evaluation Agency (EMEA) and European Medicine Agency (EMA) regulate the licensing and authorization of drug use in aquaculture for countries under EU. In Australia, application of drugs in aquaculture is regulated under 'The Commonwealth Agricultural and Veterinary Chemicals (Administration) Act' (1992, as amended in 2005) establishes the Australian Pesticides and Veterinary Medicines Authority (APVMA).

Additionally two international agencies are also working to develop standards for application of veterinary drugs in animals including fishes. The Codex Alimentarius Commission (CAC) is a joint FAO / WHO commission charged with developing standards for food safety with world wide application. The VICH (International Co-operation on Harmonisation of Technical Requirements for Registration of Veterinary Medicinal Products) is a trilateral (EU-Japan-USA) programme aimed at harmonising technical requirements for veterinary product registration. In similar lines major fish production countries in the world have their own national regulatory agency or they are the signatory to any one of the international organizations. Unfortunately no such system exists in India.

In the absence of any regulatory body, the drugs are being used without any scientific guidance and several researchers are publishing shallow information which is degrading the Indian aquaculture industry. Since, there is no programme on regulating and authorizing use of drugs in aquaculture, scanty unscientific information is being used to project the harmful effects of antibiotics in aquaculture. There is no scientific data available on the safety, efficacy, withdrawal period of drugs for use in different species of aquatic animals cultured in India. This information is essential to regulate the usage of drugs in aquaculture and to demonstrate the safety of fishery products from India. Such information will install confidence in domestic and international consumers.

Lack of data on aquaculture drug usage and scientific advisories has created unfounded concerns regarding the quantum of drugs used in fish culture, safety of cultured animals to humans and the impact of discharge water on receiving environment. To develop an efficient regulatory mechanism extensive scientific data is required in variety of aquatic species cultured in Indian farming systems. Based on such information guidelines can be developed to approve drugs which are safe, effective and has minimal adverse impact on the receiving environments in Indian aquaculture. The system may also regulate the quality at manufacturing level and suitable labelling to avoid misuse of the drugs by farmer level.

Unintended use of these substances by the fish farmers leads to residues in harvested crop, facing rejection at international market in addition to the possible threat to domestic consumers. Based on several meetings and discussions, FAO has suggested the need to follow good aquaculture practices and responsible and prudent use of safe veterinary drugs. Literary survey suggests that information on authorization procedures, control of antibacterial substances, standards of residues in aquaculture produce and international trade restrictions is lacking in public domain.

Standard process of drug approval includes target animal safety, efficiency, human food safety, quality of drug and impact on environment. Drugs commonly used in aquaculture can be classified into disinfectants, antibiotics, anti-parasitics, hormonal preparations and nutritional supplements. In the project two disinfectants (chlorine and formalin), two antimicrobials (oxytetracycline hydrochloride and sulfadimethoxine & ormetoprim) and one antiparasitic drug (Emamectin benzoate) have been selected as candidate drugs for conducting preliminary evaluation studies such as bio-safety, withdrawal period, efficacy and environmental impact.

Under the project major candidate species of aquatic animals cultured in India like, rohu (*Lobeo rohita*) and catla (*Catla catla*), silver carp (*Hypophthalmichthys molitrix*), grass carp (*Ctenopharyngodon idella*) and common carp (*Cyprinus carpio*). ***Pangassius,*** Groupers, Rainbow trout (*Oncorhynchus mykiss*) and Mahaseer, mrigal (*Cirrhinus cirrhosis / C. mrigala*), Mozambique tilapia (*Oreochromis mossambicus*) and Nile tilapia (*Tilapia nilotica*) have been selected to conduct the experiments in two seasons as the temperature is the main factor which determines the drug metabolism as fish are poikilothermic in nature and the withdrawal period is calculated as degree days. The project includes eight ICAR institutes under Fisheries division and two state agriculture universities, Navsari Agriculture University (NAU), Navsari, Gujarat and West Bengal University of Animal and Fisheries Sciences (WBUAFS), Kolkata, West Bengal.

PROJECT ACTIVITY

Lead Institute

Central Institute of Brackishwater Aquaculture (CIBA), Chennai

Commercial viability of the Indian aquaculture industry depends on the productivity and environmental safety. Economic compulsions have forced the industry to take up the intensification which needs to be backed up by scientific application of farm inputs. Unregulated aquaculture medicine market has created infusion of spurious drugs in the market without any scientific validation. In order to address the need for regulation of aquaculture medicines the All India Network Project was conceptualized. There is also a need for taking up the economic losses due to diseases so that suitable control measures can be developed.

Main objectives of the project are to classify the drugs used in aquaculture and evaluate safety of commonly used drugs in economically important species of freshwater, brackishwater and marine systems. Based on the information generated in the project the guidelines for approval of the aquaculture drugs will be developed. Project is also envisaged to popularize the better management practices, biosecurity and HACCP principles. Further, economic loss caused by disease will be assessed using modern tools to establish the commercial value for damages caused by the disease.

Partner Institutes

ICAR-Central Marine Fisheries Research Institute (CMFRI)

Classification and categorization of aquaculture drugs/chemicals used in aquaculture and economic losses due to diseases in economically important cultured species of aquatic animals is being carried out in Kerala. To address the food safety concerns of aquaculture drugs, evaluation of efficiency (dose and schedule), determination of withdrawal period and residues in aquaculture sediments and water for oxytetracycline and emamectin benzoate is being conducted in Groupers. Additionally, screening of imported marine ornamental fish for OIE listed pathogens in quarantine/hatchery facilities is also being conducted Awareness programmes to popularize biosecurity protocols and BMPs are organized to stakeholders and communicate through advisories in regional languages.

ICAR-Central Institute of Fisheries Education (CIFE)

The institute is involved in classification and categorization of aquaculture drugs/chemicals used in Maharashtra, Punjab, Haryana, Goa, Telangana, & AP (East & West Godavari, Karnool, Ananthapur). To address the food safety concerns evaluation, determination of withdrawal period and residues in aquaculture sediments and water for oxytetracycline and emamectin benzoate is being conducted in silver carp, grass carp and common carp. Additionally to popularizing biosecurity protocols and BMPs, awareness programmes / meetings, training programmes are being conducted for stakeholders. Advisories are also being prepared and distributed in regional languages. Information on economic loss due to infectious diseases is being conducted in freshwater major carps in above mentioned states.

ICAR-Central Institute of Freshwater Aquaculture (CIFA)

The institute is conducting survey for collecting data on medicines/ drugs/ chemicals being marketed for use in aquaculture from Odisha, Chhattisgarh, Jharkhand and Andhra Pradesh. Similarly the information economic loss due to disease in major cultured species of freshwater aquaculture is also being collected. CIFA is also conducting biosafety, pharmacokinetics and pharmacodynamics assay of oxytetracycline and emamectin benzoate in rohu and catla. To develop better management practices (BMPs) for decreasing pathogen loads in aquatic systems, survival period of pathogens based on soil conditions being evaluated. Dose of chemicals and disinfectants for treatment is being standardized and advisories in regional languages are being prepared for distribution among stakeholders. Training programmes are being conducted for hatchery operators and grow out culture farmers on application of HACCP principles. In collaboration with state Directorate of fisheries in Chhattisgarh, Jharkhand, Odisha and Andhra Pradesh, farmers meeting/ awareness programmes are being conducted to discuss various issues and to sensitize the farmers on wise use of drugs and chemicals in aquaculture.

ICAR-Central Inland Fisheries Research Institute (CIFRI), Kochi

The research team at ICAR-CIFRI is investigating incidence of diseases, economic loss from diseases, as well as drugs used in aquaculture in major reservoirs & wetlands of Assam and ponds & reservoirs of Karnataka, beside popularization of health management practices/BMPs among stakeholders. For sustainable cage culture, the team is also investigating diseases in *Pangasius* in cages and determining safe and effective dosages of oxytetracycline for disease management in *Pangasius*.

ICAR- Central Institute of Fisheries Technology (CIFT), Kochi

The institute is addressing food safety concerns of aquaculture drugs through generating database on residues in aquaculture produce and estimating of different drug residues in samples submitted by participating centers of the project. The institute is NABL accredited and National Referral lab for antibiotic analysis. CIFT assist CIBA in development of guidelines for the approval of aquaculture drugs chemicals which is to be prepared in consultation with farmers/stakeholders, drug control authorities and regulatory agencies (CAA). In collaboration with CIBA, HACCP protocols are being prepared and training programmes/workshops for hatcheries and grow out farms are being conducted.

ICAR-National Bureau of Fish Genetic Resources (NBFGR), Lucknow

The institute is conducting collection of data on medicines/drugs and testing kits used in aquaculture through questionnaire based survey and to assess the economic impact of major fish diseases in the state of Uttar Pradesh.

ICAR-Directorate on Coldwater Fisheries Research (DCFR), Bhimtal

The institute is conducting biosafety, pharmacokinetics and pharmacodynamics assay of oxytetracycline and emamectin benzoate in fingerlings of rainbow trout and golden mahseer. Efficacy of OTC in controlling *A. hydrophila* and *A. caviaein* rainbow trout and mahaseer is also being evaluated. Surveyed for classification and categorization of chemicals used in aquaculture is being conducted in seven states (Manipur, Tripura, Meghalaya, Arunachal Pradesh, Uttarakhand, Sikkim and Himachal pradesh). Oxytetracycline residue is being monitored in rainbow trout and golden mahseer from Uttarakhand and Himachal Pradesh. Survey for economic loss assessment due to infectious diseases is also being conducted in Sikkim and Arunachal Pradesh.

West Bengal University of Animal and Fisheries Sciences, Kolkata, West Bengal

University is involved in classification and categorization of aquaculture drugs/chemicals and by collecting required information from the state of West Bengal. Food safety concerns of aquaculture drugs like, oxytetracycline and emamectin benzoate is being addressed by evaluating efficiency, withdrawal period and residues in aquaculture sediments and water in yard experiments with Mozambique tilapia and Nile tilapia. Since West Bengal is bordering with Bangladesh screening for exotic finfish and shellfish pathogens in being carried out. Biosecurity protocols and BMPs are popularized by conducing awareness programmes/meetings/training programmes for stakeholders and providing advisories in regional languages. Survey is being conducted to document the data on economic loss due to aquatic animal diseases in the state of West Bengal.

Navsari Agriculture University (NAU), Navsari, Gujarat

As a network partner institution from Gujarat region study on economic losses due to disease in aquatic animals and survey of drugs and medicines used in shrimp farming in the state of Gujarat, Rajasthan and Madhya Pradesh will be carried out. Studies on biosafety, efficiency and withdrawal period determination will be conducted for oxytetracycline and emamectin benzoate in Indian major carp, mrigal. Training programmes for farmers and farm technicians to create awareness about the judicious use of drugs and chemicals in aquaculture are being conducted.

CLASSIFICATION OF ANTIBIOTICS USED IN FOOD PRODUCTION

K. Ashok Kumar and T.V. Sankar

ICAR - Central Institute of Fisheries Technology, Kochi, Kerala

Antibiotics are drugs of natural or synthetic origin that have the capacity to kill or to inhibit the growth of micro-organisms. Antibiotics that are sufficiently non-toxic to the host are used as chemotherapeutic agents in the treatment of infectious diseases of humans, animals and plants. They have long been present in the environment and have played a crucial role in the battle between man and microbe. Many bacterial species multiply rapidly enough to double their numbers every 20-30 minutes, so their ability to adapt to changes in the environment and survive unfavourable conditions often results in the development of mutations that enable the species to survive changing external conditions. The indiscriminate use of antibiotics for veterinary purposes has increasingly become a matter of public concern, and legal requirements are being reinforced. Regulatory authorities license antibiotics for use if the agents meet scientific criteria for quality, efficacy and safety. The authorities have to consider safety in relation to the treated animal, to the consumer and to the individuals handling the product during treatment.

Main mechanism through which the antibiotics function involves, inhibition of cell wall synthesis, protein synthesis, nucleic acid synthesis, metabolic pathways or interference with cell membrane integrity. The National Committee for Clinical Laboratory Standards (NCCLS) has defined terms to describe herd or flock antibiotic use. Therapy is the administration of an antimicrobial to an animal, or group of animals, which exhibit frank clinical disease. Control is the administration of an antimicrobial to animals, usually as a herd or flock, in which morbidity and/or mortality has exceeded baseline norms. The feeding of antibiotics 'growth promotion' is associated with decrease in animal gut mass, increased intestinal absorption of nutrients and energy sparing. Antibiotics act by eliminating the subclinical population of pathogenic micro- organisms. Eradicating this metabolic drain allows more efficient use of nutrients for food production. Antibiotics alter the non-pathogenic intestinal flora, producing beneficial effects on digestive processes and more efficient utilization of nutrients in feeds. Some antibiotics are banned for use in food producing animals. as the residue of the antibiotic will remain in the meat and will result in the development of antimicrobial resistance. Therefore, United States of America Federal regulations prohibit its use in food-producing animals and animal-feed products According to the European Medicines Agency (EMEA) a number of antibiotics are no longer available for use in veterinarian medicine.

Antibiotics used in aquaculture can be bioaccumulative and present a food safety hazard. Aquaculture farmers who use these substances should follow product labels regarding dosage, withdrawal period, proper use, storage, disposal and other constraints including environmental and human safety precautions. Records should be maintained properly regarding the type of chemical used, its source, the quantity and withdrawal period observed. The adoption of HACCP and GMP by aquaculturists is a practical way to tackle this hazard and to show case our products to the international community as a safe and high quality product.

PHARMACOKINETICS AND PHARMACODYNAMICS OF ANTIBIOTICS IN AQUATIC ANIMALS

Satheesha Avunje and P.K. Patil

Aquatic Animal Health and Environment Division, ICAR-CIBA, Chennai

Knowledge on Pharmacokinetics (PK) and pharmacodynamics (PD) of antibiotics is very import in developing therapeutic approach. PK is study of the time course of absorption, bioavailability, distribution, metabolism, and excretion of the drug, while PD is study of the biochemical, physiologic, and molecular effects of drugs on the body and involves receptor binding, post-receptor effects, and chemical interactions. In simple terms, PK is fate of the drug in the body while PD is what drug does to the body.

Information on PD and PK of a particular drug helps in determining dose and its response. Majority of the antibiotics classes are banned for aquaculture application and for the best utilisation of the permitted antibiotics, it is very important to know their PK and PD. Antibiotics generally applied orally in aquaculture and in such a situation, their availability for assimilation and stability in the host is very important. For oral administration, bio-availability/stability of antibiotics at acidic pH should be checked. Tetracycline bind with calcium, magnesium, iron and aluminium to form insoluble complexes and hence their bio-availability is significantly reduced. The assimilated drug is distributed in the body and accumulates depending on the function of the organ/tissue and in highly blood-perfused organ. Highest drug accumulating organ will be those involved in drug metabolism and excretion such as liver/hepatopancreas and kidney. Furthermore distribution of drug into the cells depends on their lipid-solubility as the drugs have to cross through biological membrane by diffusion. Drug fed to fishes is metabolised in liver/hepatopancreas and excreted or excreted as it is either through kidney or with faecal matter. Antibiotics such as tetracycline are excreted by glomerular filtration. This also depends on the environmental temperature and salinity of the water as temperature directly affects metabolic rate while salts and ions interfere availability and accumulation of antibiotics. Efficacy of metabolism and excretion decides withdrawal period of the antibiotics and is crucial in developing therapeutic dose for fish and shellfishes. Oxytetracycline is one among the USFDA approved antibiotics and widely used drug, has a withdrawal period of six to ten days in various organs of *Penaeus vannamei* at a temperature of 28°C.

Antibiotic dosage should be decided based on the minimum inhibitory concentration (MIC) of the targeted bacteria, bio-availability, bio-accumulation and withdrawal period. When level of bacteriostatic drug is excess of MIC, bacterial count may decline due to host defence. When level of unbound bacteriostatic antibiotic is below MIC, antibacterial affect can be due to (i) post-antibiotic effect (PAE) with persistent suppression of bacterial growth, (ii) enhancing bacterial susceptibility to phagocytosis by post-antibiotic leukocyte enhancement (PALE) and (iii) by altering bacterial morphology. Based on PD, antimicrobial compounds can be classified into three groups. (i) Drugs with time-dependent bactericidal action, (ii) Drugs with concentration-dependent bactericidal action and (iii) bacteriostatic and that produce moderate to prolonged PAEs. The level of antibiotics in blood may vary from the infected tissue based on surface area of the capillary bed to the volume of the tissue compartment, the physico-chemical characteristics of the drug; hence measurement of blood antibiotic may not give actual concentration of the drug in the animal. Thus for determining drug efficacy and dosage, information about PD and PK can be crucial.

MOLECULAR MECHANISMS OF ANTIMICROBIAL RESISTANCE

Subhendu Kumar Otta and P.K.Patil

Aquatic Animal Health and Environment Division, ICAR-CIBA, Chennai

For more than 3.8 billion years, diverse microorganisms have been playing their respective roles on this earth. One fraction of such organisms are also well recognised for their detrimental effect through disease causing as well as bringing mortality to many forms of life including human beings. Discovery of the antibiotics was then accepted as a great achievement as it was able to save lives and sufferings. However, slowly and on long term basis, this has tried to come back as a boomerang and become a matter of major concern during the recent times. This is mainly due to indiscriminate use of several such antibiotics and ready unavailability of new generation antibiotics to counteract this. Though antibiotics resistance phenomenon was observed as early as 1940, it became obvious only when sufficient new generation antibiotics were not able to be synthesised to fill up the gap.

Based on either the structure or certain important functions in bacteria, the mode of action of different antibiotics has been determined. This includes inhibition of synthesis of cell wall or nucleic acid and inhibition of function for ribosome, cell membrane or folate metabolism. Subsequently microorganisms were able to counteract these actions either temporarily due to incorrect use or permanently through selection pressure. As a result, the sensitive microorganisms were subsequently replaced by the emergence of resistance ones to create havoc. This resistance development was primarily based on the chemical structure of the antibiotics and the mechanism through which they act on the target. Resistance can be either intrinsic or natural and acquired. In natural way microorganisms either do not possess the necessary target sites or having different chemical composition to avoid the permeability. Acquired resistance is either through the modification of existing ways or through the use of alternate ways on which the antibiotics cannot exhibit its function.

Microorganisms can acquire resistance through a number of ways. One of the attempts from microorganisms is to inhibit the particular antimicrobial which they were repeatedly subjected to. This function they achieve by synthesising specific enzymes that can destroy the antimicrobials. Many of the antimicrobials act on the specific enzymes synthesised by the microorganisms to carry out the required function. Therefore, microorganisms try developing alternate enzymes to carry out these functions and thereby acquire resistance to these specific antimicrobials. In order to exert its function, antimicrobials bind to specific sites to carry out the function. In such cases, microorganisms bring specific mutations on the target sites and inhibit the binding of antimicrobials. Otherwise, the microorganisms bring changes to the site through post-transcriptional modification and thereby prevent the binding of antimicrobials. In another way, the microorganisms modify the body chemical composition to reduce the uptake of antimicrobials. As the substances do not enter in desired quantity, it becomes ineffective and thereby microorganisms acquire resistance. Exactly in an opposite way, the microorganisms can also modify the body composition for active efflux of the antimicrobials. Microorganisms can also overproduce the required target sites to counteract the antimicrobials. Depending on the particular situation, microorganisms can either overexpress or supress a particular gene to nullify the specific effect of the antibiotics. Sometimes microorganisms prefer to form biofilm instead of remaining in planktonic forms and thereby avoid the penetration of antimicrobials. Many a times, the microorganisms can also develop a totally novel and previously unknown mechanism through which they can acquire antimicrobial resistance.

Once the resistance genes in the microorganisms established, these can spread and propagate in other microorganisms. This can be through horizontal gene transfer (conjugation, transformation or transduction). Pilus mediated conjugative plasmid transfer is the most effective and common way of spread of resistance genes.

The selective pressure that is caused through the antimicrobial consumption is the main concern and one of the prominent risk factor for the development of antimicrobial resistance. There is every possibility that this pattern of resistance will further increase through the indiscriminate use of antimicrobials. Food industry, of which aquaculture product is a part, can play a major role in the increase of antimicrobial resistance microorganisms which is a major concern as there is a greater chance for the transfer of resistance microbes through the food chain. Therefore, specific awareness is a need of the hour to prevent this.

ANTIBIOTIC USE IN HEALTH CARE SYSTEMS: REGULATIONS AND PRACTICES

Sujith J Chandy

Christian Medical College, Vellore, Tamil Nadu

Bacterial infections continue to be a significant contributing factor in mortality throughout the world. A major factor in controlling such infections has been the discovery of antibacterial medicines (hereafter referred to as antibiotics). However, access to effective antibiotics can no longer be taken for granted due to the phenomenon of bacterial resistance. Bacterial resistance has been defined by the CDC as "the result of bacteria changing in ways that reduce or eliminate the effectiveness of drugs, chemicals, or other agents to cure or prevent infections".

Bacterial resistance to antibiotics has become a problem throughout the world, including India. In South India, a study done in the community in Vellore in parallel to the present study showed that 42 percent of commensal *Escherichia coli* was resistant to one or more antibiotics. In this scenario, a recent study showing the presence in India of gram-negative Enterobacteriaceae with resistance to carbapenems due to New Delhi metallo-ß-lactamase 1 (NDM-1) has further put the issue of resistance in the spotlight.

There are many reasons for rise of resistance, but studies show that individual as well as aggregate antibiotic use are contributing factors. In India, the relatively few studies done reveal that prescriptions containing antibiotics vary from 26 percent, to as high as 80 percent. In 2001, WHO published the WHO Global Strategy for Containment of Antimicrobial Resistance (AMR). This document urges development of strategies to optimize antibiotic use. The need for meeting this challenge was also advocated by organizations and leading experts in this area.

This talk will focus on bringing into context the spread of the AMR phenomenon over the world and in India. The implications of AMR on humans will be dealt upon. Following this, the association of antibiotic use with AMR and its misuse will be illustrated through the findings of two studies done in India. It would be also important to dwell on the reasons why antibiotics are inappropriately used and an example of this will be disseminated through a qualitative research study. Issues such as antibiotic residue in the environment will also be touch upon.

A look at the global action plan and various broad strategies such as antibiotic stewardship and regulatory strategies would then be done. Antibiotic stewardship is currently being implemented in a few major hospitals in the country, but many of the smaller hospitals have not implemented it fully. Do policy guidelines work? This is another question that will be discussed. Some weaknesses and strengths in such strategies and what could be implemented in India for improving antibiotic use in humans will also be discussed. It is hoped that this talk will give an overview of the issues of antibiotic use in humans so as to complement the one health approach.

ROLE OF NON-HUMAN USE OF ANTIBIOTICS IN DEVELOPMENT OF RESISTANCE IN BACTERIAL PATHOGENS OF PUBLIC HEALTH IMPORTANCE

Padma Krishnan

Institute of Basic Medical Sciences, University of Madras, Chennai.

In recent years, much emphasis has been given to the public health impact of non-human use of antibiotics which is difficult to quantify. Dissemination of antibiotic resistance arising due to non-human use has three different routes namely- consumer route, occupational route and agricultural route. Bacteria that are capable of colonization and opportunism (*E. coli*, *Klebsiella*, *S. aureus* and *C. difficile*) called as Colonizing Opportunistic Pathogens (COPs) are important in the acquisition and dissemination of antibiotic resistance in non-clinical settings. Among the different non clinical environments, antibiotic use among food producing animals for therapeutic and non therapeutic purposes has caused a serious concern increasing the probability of resistant gene capture event and dissemination.

Role of integrons in antibiotic resistant trends and diversity of class 1 integron gene cassette among enterobacterial isolates of animal and environmental origin : Dissemination of antibiotic resistance in non clinical settings due to the non-human use of antibiotics is driven by mobile genetic elements, plasmids and specific clones (ST). Integrons are archaic genetic structures that co-evolved along with the rise in antibiotic resistance in Gram negative bacilli. Analyzing these elements in different ecological niches will provide an insight into the more complex and complicated process of resistant gene capture and dissemination in Gram negative bacilli. In our study, we have analysed the diversity of class 1 integron gene cassette among enterobacterial isolates of human clinical, animal origin and environmental sources which included water bodies in Chennai.

Incidence of Antibiotic Resistance in Broilers and its Impact on Public Health: The use of antibiotics at sub-therapeutic concentrations in poultry farm is believed to be an important factor for development of **antibiotic resistance genes (ARGs)** thereby resulting in proliferation of antibiotic-resistant bacteria in farm environment. ARGs are emerging environmental contaminants and pose a threat to human health. Our study was undertaken to determine the prevalence of resistance in staphylococcal and enterobacterial isolates to antibiotics commonly used as growth promoters in poultry farms. Further, the persistence of antimicrobial resistance genes in poultry farm soil was also assessed.

ANTIBIOTIC USAGE PATTERNS IN ANIMAL HUSBANDRY AND FOOD SAFETY: REGULATIONS AND PRACTICES

S. Ramesh

Tamil Nadu Veterinary and Animal Sciences University (TANUVAS), Chennai

Antibacterial agents occupy an important position in the treatment of infectious diseases in man and animals. Quantitatively, they are one of the most widely used classes of drugs. Thanks to the arrival of these agents, infectious agents are no more a major threat and mass deaths due to bacterial infections have become history.

Animal farming such as dairy, poultry and piggery have become a big industry leading to a big leap in the supply of animal protein across the globe. Gross production practices necessitate intensive systems of farming. A major fall out of this is the increase in infectious diseases due to overcrowding of animals. In countries like India, where the optimal bio-security cannot be maintained in animal farms, antibacterial drugs remain the mainstay in the treatment of infections. Poultry, dairy cattle, pigs and small ruminants are some of the species where they are commonly used. Antibiotic usage in animals occupies a very important position in terms of quantity of antibiotics used.

How antibiotics are used in animal production?

Therapeutic: The therapeutic treatment of individual sick animals with antibiotic drugs is often essential. It relieves suffering and returns them to economic production. This is more common in larger species where single or a few sick animals necessarily have to be treated to relieve suffering and also to return the animals to optimal production at the earliest.

Metaphylactic: This is practiced in smaller species such as poultry where it is often difficult to carry out individual treatments. On the face of an infection in the herd / flock, all the animals in the farm, including those that are healthy are treated with antibiotics. This, causes unnecessary exposure to antibiotics rendering them not effective, in future cases.

Prophylactic: The treatment of animals with low, sub-therapeutic doses of antibiotics in feed or drinking water, when they are not showing signs of disease but there is thought to be a risk of infection. Treatment can be over a period of several weeks, and sometimes longer.

Growth promotion: Very low sub-therapeutic doses of antibiotics are given to animals (particularly pigs and poultry) in their feed, to increase their growth-rate and productivity. Treatment is continuous and can last for a large part of the animal's life.

Issues in antibiotic use in livestock and poultry: While therapeutic regimens of antibiotics are often necessary from the point of relief of suffering, cure of disease and prevention of disease spread, other modes of usage have created an undesirable situation. Such unwarranted excessive usage has been incriminated to be a major source of antibiotic resistance, a grave threat faced by all the nations. This compounds the excessive usage of antibiotic usage in humans, leading to a scenario where these wonderful drugs are losing their efficacy.

Resistance to antimicrobial drugs; Resistance to drugs is not a new phenomenon. As the usage of antibiotics increase resistance is bound to occur. Resistance was reported for penicillin in the same year it was introduced. Likewise reports of resistance to other antimicrobials, within a few years of their introduction. But the fact that there has been a steady increase in the occurrence of resistance across species especially against the most important life saving drugs has becoming a factor of major concern for health professionals and planners.

Resistance to fluoroquinolones in Campylobacter isolated from poultry; widespread prevalence of Extended spectrum betalactamases (ESBL) from livestock sources; isolation of MRSA from livestock and poultry etc. are some of the significant findings that leave the Governments across the globe genuinely worried about the utility of antimicrobials in the future.

Antimicrobial residues: Livestock and poultry constitute an important source of food such as meat, milk and egg. As the animals are frequently exposed to antimicrobials, residues of these drugs find their way into the foods of animal origin. Residues of antimicrobials in foods can cause adverse effects, mild or severe and rarely leading to fatalities too. Since many of the infections of animals can cause disease in the human beings , low levels of residues will lead to prevalence of resistant bacteria. The residues in animal foods can also mean spread of resistant bacteria into the environment such as soil and water.

From a regulatory point of view, production of safe foods entails strict adherence to the Maximum Residue Limits (MRLs) and withdrawal periods of drugs in the respective products as outlined in the law.

No new drugs in the pipeline: While the 'Golden era' of chemotherapy saw the arrival of numerous drugs that act by different mechanisms leading to a huge success over infections, the last two decades have seen the inflow of new drugs to a trickle. With the existing drugs slowly losing their efficacy we may be left to wage a losing war against many infections in man and animals.

Mitigatory measures : Health professionals, law makers and stakeholders are grappling with the menace of excess antibiotic use. This has become one of the major issues affecting both the developed and the developing world. Agencies like FDA, WHO, OIE etc. periodically assess the situation globally and suggest measures regularly to overcome this problem. A lot of concerted effort is required to create awareness among all stakeholders, implement measures to minimize the impact and prolong the utility of the existing antibiotics. The measures suggested by scientific world and the regulations brought about by lawmakers will be discussed.

ANTIBIOTIC USAGE PATTERNS IN AGRICULTURE AND FOOD SAFETY: REGULATIONS AND PRACTICES

V. Paranidharan

Tamil Nadu Agriculture University, Coimbatore, Tamil Nadu.

Antibiotics have been used since the 1950s to control certain bacterial diseases of high-value fruit, vegetable, and ornamental plants. Today, the antibiotics most commonly used on plants are oxytetracycline and streptomycin. Antibiotics are essential for control of bacterial diseases of plants, especially fire blight of pear and apple and bacterial spot of peach. Streptomycin is used in several countries; the use of oxytetracycline, oxolinic acid and gentamicin is limited to only a few countries. Springtime antibiotic sprays suppress pathogen growth on flowers and leaf surfaces before infection; after infection, antibiotics are ineffective. Antibiotics are applied when disease risk is high, and consequently the majority of orchards are not treated annually. Antibiotics are active on plants for less than a week, and significant residues have not been found on harvested fruit. Antibiotics have been indispensable for crop protection in the United States for more than 50 years without reports of adverse effects on human health or persistent impacts on the environment. Resistance of plant pathogens to oxytetracycline is rare, but the emergence of streptomycin-resistant strains of *Erwinia amylovora,Pseudomonas* spp., and *Xanthomonas campestris* has impeded the control of several important diseases. A fraction of streptomycin-resistance genes in plant-associated bacteria are similar to those found in bacteria isolated from humans, animals, and soil, and are associated with transfer-proficient elements. However, the most common vehicles of streptomycin-resistance genes in human and plant pathogens are genetically distinct. Nonetheless, the role of antibiotic use on plants in the antibiotic-resistance crisis in human medicine is the subject of debate. Recognizing a potentially diverse readership, such as practical aspects of antibiotic use on plants, specifically that the diversity and quantity of antibiotics applied to plants is small relative to uses in human and veterinary medicine. The body of knowledge on the molecular genetics of antibiotic resistance in plant-associated bacteria to propose routes of horizontal gene transfer that might explain the widespread occurrence of homologous resistance genes in diverse bacteria. The role of antibiotic use on plants is probably insignificant but, we need more research for further confirmation.

ANTIBIOTIC USAGE PATTERNS IN SERICULTURE FOR PRODUCTIVITY ENHANCEMENT

Bhaskar, R. N. and Anusha, H. G.

University of Agricultural Sciences (UAS), Bengaluru

There are many factors that influence on the success of production of silk. Growth and development of larvae depends on the intricate physiological processes that take place in the silkworm. In recent years administrations of antimicrobial agents have been used for controlling of silkworm diseases and improve production of silk. Antibiotics administration resulted in harvesting of superior cocoon crop and controlling the silkworm diseases. Therefore improvement of silk quality means improvement of the feed nutrition and upkeep of the larval health, since silkworm is highly susceptible to infection caused by major pathogenic groups. Antibiotics are among the most frequently advocated medications in modern medicine which show promising results in controlling bacterial and viral diseases in animals including insects. Further use of broad spectrum antibiotics viz., penicillin, streptomycin, tetracycline and chloramphenicol were already tried on silkworm and found successful. The oral supplementation of the antibiotics Amoxicillin to fourth instar larvae resulted significant increase in larval weight, cocoon weight, shell weight, shell ratio, filament length and Denier. In addition oral administration of Streptomycin and Penicillin increased the meterage of reelable silk. Fecundity was found to be more after Campicillin, Cloxacillin and Chloramphenicol treatments. In vitro use of streptomycin sulfate @ 1000 ppm proved successful control of bacterial diseases in Muga silkworm up to 52.37 per cent. The antibiotics like Penicillin, Ampicillin and Streptomycin were found to be effective in reducing the mortality of silkworms by 23-25 per cent without affecting the cocoon parameters. Further, use of antibiotics in silkworm nutrition establishing the silkworm as an effective tool for experimentation in the existing system of pathogen studies and drug screening.

CHALLENGES IN REGULATING USE OF ANTIMICROBIAL AGENTS IN INDIAN AQUACULTURE

P.K.Patil, Satheesha Avunje and K.K. Vijayan

Aquatic Animal Health and Environment Division, ICAR-CIBA, Chennai

Generally drugs are used in aquaculture for treatment and prevention of disease, controlling parasitic infestations, regulation of reproduction and growth and tranquilizing aquatic animals for weighing or transportation. Very few drugs are approved for use in aquaculture in countries where the regulation exists and no such regulations present in most of the developing countries including India. This has lead to use of unapproved drugs or misuse of approved drugs in aquaculture posing potential risk to human health. Development of antibiotic resistance is considered as a major risk factor in addition to possible toxicity, allergy or carcinogenicity to humans. Establishment of regulations and guidelines are the key for reducing the risk of antimicrobial resistance arise out of aquaculture activities. In the public health interest the several international organizations have recommended the responsible and prudent use of veterinary antimicrobial agents in aquaculture. Food and Drug Administration (FDA) Center for Veterinary Medicine legally approves the use of drugs and chemicals for aquaculture use in the US. There are only three FDA approved antimicrobial agents, oxytetracycline HCl, sulfamerazine and a combined preparation that contains sulfadimethozine and ormetoprim for use in aquaculture. Information on composition of the commercial product, target species, route and schedule of application, tolerance limits and withdrawal periods for each target species is also provided by CVM of FDA. The drugs intended for aquaculture have been classified as approved, low regulatory priority, high enforcement priority and prohibited for extra label use. Similar aquaculture drug usage guidelines exist in the EU, UK, Japan and other countries.

To address the issue of antimicrobial resistance special emphasis needs to be given to effective disease diagnosis, factors inducing environmental stress and sound understanding of biological and chemotherapeutic agents and rational selection of prophylactic mitigatory measures. Though information on disease diagnosis and BMPs are available for aquaculture activities, data on the quantities of antimicrobial agents used and the standard methodologies to be followed for their application in aquaculture is not available in India. This has lead to presumption by the international agencies about the improper use of these substances in Indian aquaculture.

Such regulatory guidelines are essential for Indian aquaculture and effort is being made under ICAR funded All India Network project on Fish Health which is a consortia of eight ICAR institutes under fisheries division and two state agriculture universities. Concerted effort is being made to develop information on safety, efficiency, dose, schedule, withdrawal period for selected group of drugs in candidate aquatic animal species. Further there is an urgent need to develop programmes to monitor antimicrobial resistance patterns in microbes isolated form cultured aquatic animals and their environment and national level awareness campaign to among multiple stakeholders involved in aquaculture in India.

DETERMINATION OF ANTIBIOTIC RESIDUES IN FISH/MEAT

T. V. Sankar and K. Ashok Kumar

ICAR-Central Institute of Fisheries Technology, Kochi

The wide spread use of antibiotics in the food producing animals at various stages is a concern as this may lead to the development of resistant human pathogens. A large increase in the demand for seafood products has led to a concomitant increase in high intensity aquaculture methods and heavy use of formulated feeds containing antibiotics, among other substances. Therefore, accurate and sensitive determination of antibiotic residues is absolutely necessary to protect human health and many regulatory organizations and counties have established maximum residue limits (MRL) for antibiotic residues in animal products entering the human food chain.

Antibiotic residues in fish and fishery products are estimated after extraction with buffer/organic solvents depending on the types of antibiotics, purified and estimated by LC-MS/MS method. Liquid chromatography–mass spectrometry is an advanced analytical instrumental technique that combines the physical separation capabilities of liquid chromatography with the mass analysis capabilities of mass spectrometer. The system can selectively detect compounds of interest in a complex matrix, thus making it easy to find and identify molecules at trace levels.

Legislation by EU for antibiotic residues for sulfonamides Parent drug the MRL is 100 µg/kg and among Tetracyclines group the maximum residual level is same for all the three antibiotics namely chlortetracycline, oxytetracycline and tetracycline (sum of parent drug and its 4- epimer) is 100 µg/kg.

Estimation of Tetracyclines: Tetracyclines are difficult to analyze due to their instability, their tendency to form chelation complexes with multivalent cations, their ability to bind with proteins, and their ability to interact with charged silanol groups on silica-based sorbents. TCs exist as zwitterions at pH 4 and are in their most stable state. At this pH it is possible to sufficiently deproteinise biological samples. In this method the extraction solution is 5 percent TCA, which helps to denaturate the proteins and maintain the pH in acidic range.

The tetracycline group includes Tetracycline, Chlortetracycline and Oxytetracycline. For the purpose of analysis, a 1000ppm stock solution in Methanol:Water (1:1) was prepared and a working Standard of 1ppm in 25 percent acetonitrile containing 10mM oxalic acid was used for analysis. For the extraction of tetracyclines from fish meat, 5g homogenized meat was extracted with 10mL of 5 percent TCA, vortexed and sonicated for 10min. After centrifugation the supernatant was filtered through 0.2µm PTFE membrane and analysed by LC-MS/MS. For recovery studies, 5g homogenized meat is spiked with appropriate concentration of standards (100ppb tetracycline standard mixture) and extracted as above and analysed using LC-MS/MS.

In an alternate method using 2.5g of homogenized sample is extracted with EDTA Mcllvaine buffer pH 4 was added, vortexed and centrifuged 6000 rpm for 7min at 8oC. The supernatant is collected and the meat is extracted twice more and the combined supernatant is treated with1mL 20% TCA, vortexed and centrifuged at 6000rpm for 15min at 8°C. The supernatant was subjected to SPE clean up. Evaporated the eluted sample and reconstituted with 0.1 percent TFA in water: 0.1 percent TFA in methanol (1:1). After filtration the sample was analyzed by LC- MS/MS. For recovery studies, 2.5g of homogenized sample is spiked with appropriate concentration of standards (100ppb tetracycline standard mixture),extracted with EDTA Mcllvaine buffer pH 4 as above and analyzed by LC- MS/MS.

Estimation of Sulfonamides: For sulfonamides such as Sulfadimethoxine, Sulfamerazine, Sulfadiazine, Sulfamethazine, Sulfamethizole, stock solution of 1000ppm in Methanol: Water (1:1) and a working Standard of1ppm in 25 percent acetonitrile with 10mM oxalic acid was prepared for analysis. For extraction, to 5g of homogenized meat 5mL of water was added and vortexed. Then 10mL of acidified acetonitrile (1% acetic acid in acetonitrile) was added followed by the addition of Quechers salt. After mixing well and centrifugation, the homogenate is filtered and supernatant was analyzed by LC-MS/MS. For recovery studies, 5g of homogenized meat was spiked with appropriate concentration of standard mixture and proceeded as above.

FATE OF ANTIBIOTICS IN ENVIRONMENT

Kumararaja, R. Saraswathi, P.K. Patil, N. Lalitha and M. Muralidhar

Aquatic Animal Health and Environment Division, ICAR-CIBA, Chennai

Aquaculture is the fastest growing food producing sector and it accounted for 46% of total food fish supply. Intensification of aquaculture resulted in the conditions favourable to the development of diseases. Consequently, a wide range of chemicals are used in aquaculture for the control of diseases and improvement of growing environment. Antibiotics are synthetic or semisynthetic products that are used to kill or inhibit bacteria, fungi or viruses and their use has increased in recent years. The antibiotics are grouped into different classes such as tetracycline's, sulfonamides, macrolides, B-lactams, etc. based on their variation in molecular structures and physico-chemical properties. A sizeable fraction of the antibiotics are released into the environment due to incomplete absorption and metabolism in target organisms.

Mode of application, physico-chemical properties of antibiotics as well as environment affect the fate and persistence of antibiotics. The unabsorbed antibiotics from the bathing treatment enter into the environment as effluent. Antibiotics applied through feed supplement may loss either by leaching prior to ingestion by animal or through elimination by the animal metabolism in the faces or urine. The antibiotics reaches to the environment depends on its bioavailability which vary with the environmental characteristics as well as properties of antibiotics. Partitioning is the important process determines the fate of antibiotics in the environment. Sorption and desorption are mechanisms responsible for the partitioning of antibiotics between water phase and sediment phase and the bioavailability to aquatic biota. The bioavailability of Oxytetracycline is less than 10 percent in marine system due to its chelation by the divalent metal ions ($Ca2+$ and $Mg2+$) which reduces the lipid transferability. Lalumera et al. (2004) found that 75 percent of the given drug is released from the body of the fish through secretions as a non-metabolite molecule, which directly discharges into the aquatic environment.

Hydrolysis and photolysis are the two major abiotic degradation pathways of antibiotics. Acidic pH is most suitable for the hydrolysis of sulphonamides and it increases with increase in temperature. Under acidic condition sulphonamides hydrolysed to sulfanilic acid and amino derivatives. Under natural environmental condition sulphonamides are hydrolytically stable with longer half-life. Tetracylines are highly sensitive to hydrolysis and affected by temperature, pH etc. The relatively high water solubility of OTC makes it prone to hydrolysis. The hydrolysis rates for Oxytetracycline increase as the pH level deviates from pH 7 and as temperature increases. Fluoroquinolones are insensitive to hydrolysis. As macrolides are weak bases, they are unstable at acidic condition. Fluoroquinolones and sulfonamides are resistant to hydrolysis at natural environmental condition of pH 7-9. Photolysis is efficient only in the surface water and negligible at deeper layers. Tetracyclines are liable to photolysis and sulfonamides are photo resistant. The main degradation mechanism for OTC in the environment is considered to be through photodecomposition which is enhanced by the light intensity. The half-life of oxolinic acid under natural illumination in shrimp pond water was reportedly 2.3-4.8 days and oxytetracycline was

21 days. Thus, the tetracyclines tend to degrade quite rapidly under conditions similar to those encountered in natural water and lagoons.

Accumulation of antibiotics in sediments can occur either as a result of direct deposition of treated feed pellets or by adsorption of antibiotics in dissolved or colloidal form onto settling particles. Physico-chemical properties of both antibiotics and environment affect the partitioning to sediments and degradation. The environmental factors such as climate, pH, redox condition of water and sediment components affect the persistence of antibiotics. As most of the antibiotics are weak acids, weak bases or zwitterions not only hydrophobic interactions but also cation exchange, cation bridging, surface complexation and hydrogen bonding contribute to sorption. Sorption affected by amount and nature of suspended solid particles in water phase and water/sediment properties such as pH and organic matter content. The order of sorption capability of antibiotics follows the order: Fluoroquinolones ⩾ Tetracyclines > Macrolides > Sulphonamides.

Besides chemical and photochemical degradation, the biodegradability of antibiotics, i.e. their susceptibility to decomposition by living organisms, is another important factor. In fact, most fluoroquinolones are considered not to be bio transformed or biodegraded. It has been postulated that the high fixation rates of fluoroquinolones and tetracycline compounds to the surface or in pores of the sediment matrix may effectively protect them from biodegradation.

The over-use of antibiotics has led to an increase in antibiotic resistance among bacteria populations. This leads directly to a decrease in the effectiveness of antibiotic usage for targeted organisms and affect the biota of the environment.

INDIAN SHRIMP TRADE IN INTERNATIONAL MARKETS AND TECHNICAL BARRIER MEASURES OF ANTIBIOTICS AND OTHER SANITARY AND PHYTO SANITARY (SPS) MEASURES

T. Ravisankar and S. Vinoth

Social Science Division, ICAR-CIBA, Chennai

International trade in market place is always pitched on fair bilateral relations and zero or positive balance of payments between importing and exporting nations. Food safety, environmental and ethical concerns are used as masks of enforcing the former objectives on many occasions. World Trade Organization exists to ensure that international trade flows as smoothly, predictably and freely as possible, benefiting producers and consumers in the world. But though tariff measures like anti-dumping duty can be contested in WTO, use of non-tariff barriers particularly of non-protectionist type of policies, to curtail import from a particular country, leave little scope for litigation. Invoking the health and safety of people, animals, and plants; to protect or improve the environment makes the opposition blunt. Licensing, packaging, and labeling requirements; sanitary and phytosanitary (SPS) rules; food, plant and animal inspections; import bans based on objectionable fishing or harvesting methods are technical barriers put up by importing nations. These lead to limited formal consequences in the guise of efforts to establish common standards or mutual recognition of different standards.

Rejection of primary products from agriculture, livestock and fisheries on the account SPS measures have been used effectively by importing nations to brand producer nations as irresponsible towards food safety, environment and ethics. The statistics are often misinterpreted without giving a full picture. It is widely reported in press large number of Indian shrimp consignments are rejected in 2015 due to antibiotic residues. Indian shrimps were imported by USA in Jan to Dec 2015 to the tune of 1, 35,352 metric tons out of total USA import of 5,85,826 metric tons. This accounts for 23.10 percent of total shrimp imports to USA. In the same period (Jan – Dec 2015) the total rejection of shrimp lines (consignments) from different countries were 389 and rejection of Indian consignments were only 34. Let us try to approximately index this against the total export from India in 2015. The Indian shrimp exports would have been received roughly in 6800 containers of 18 to 20 tons each by USA ports and detection of antibiotic residues was reported only in 34 consignments (0.5 per cent). These rejections were from less than half a dozen exporters from Bhimavaram, Kochi and Chennai. But the data is blown up out of proportion as if all Indian shrimp farmers violate the codes of responsible farming.

The uses of technical barriers like antibiotic residues are used to protect domestic shrimp industry by importing countries. Prescription of too stringent standards for import items is a normal method of restricting cheaper imports and to protect incompetent domestic production. These measures are normally affecting consumers of importing country as much as producers from exporting countries. Hence Indian shrimp industry, apart from imposing self-regulations on responsible antibiotic use, should also lobby with consumers of importing countries including large retail chains through which the commodity is channelized to reach the final consumers.

ALTERNATIVES TO ANTIBIOTICS IN AQUACULTURE

R. Ananda Raja, S.K.Otta and S.V.Alavandi

Aquatic Animal Health and Environment Division, ICAR-CIBA, Chennai

As the world's population continues to climb exponentially, the demand for producing food production remains challenging. New innovative sustainable technologies are need of the hour in agriculture, animal husbandry and fishery sector as a whole. As the new technologies emerge for increasing the food production, the parallel increase of problems associated mainly with the infectious diseases is inevitable. The usage of antibiotics in aquaculture poses great threat by interaction with other environmental contaminants and development of antibiotic resistance. Vaccination is an ideal method for preventing infectious diseases, but it is not a treatment for existing infections, and commercially available vaccines are still very limited in the aquaculture field. The rise in bacterial antibiotic resistance and antibiotic residues has become global concerns, and there is a need to develop alternative therapies for bacterial pathogens in animal production, especially in aquaculture.

Age-segregation, all-in all-out management, biosecurity, sanitation, zero water exchange and vaccination are just a few examples of no antibiotic practices that may be used in the prevention and control of many infectious diseases in aquaculture. But, none of these measures is sufficient to completely eliminate the bacterial infections on most farms. Further, many research findings reveal that there is a scope with probiotics, prebiotics, immunostimulants, essential oils and bacteriophages to combat some infectious viral and bacterial diseases.

Probiotics: The use of innocuous live microorganisms to avoid bacterial infection in aquaculture has a beneficial effect on the host by modifying the host-associated or ambient microbial community, by ensuring improved use of the feed or enhancing its nutritional value, by enhancing the host immune response towards disease, or by improving the quality of its ambient environment. Some probiotics reside in the digestive tracts of the individuals while others have an external origin. Probiotics that are currently used in aquaculture industry include a wide range of taxa viz, *Lactobacillus* spp., *Bifidobacterium* spp., *Pediococcus* spp., Streptococcus spp. *Carnobacterium* spp., *Bacillus* spp., *Flavobacterium* spp., *Cytophaga* spp., Pseudomonas spp., *Alteromonas* spp., *Aeromonas* spp., *Enterococcus* spp., *Nitrosomonas* spp., *Nitrobacter* spp., *Vibrio* spp., yeast (*Saccharomyces* spp., *Debaryomyces* spp.), etc.

Prebiotics: Prebiotics are the indigestible components present in the diet which are metabolized by specific microorganisms which prove to be helpful for growth and health of the host. Prebiotics shift the microbial community to one dominated by beneficial bacteria, such as *Lactobacillus* spp. and *Bifidobacterium* spp. Most efficient prebiotics which find their application in the field of aquaculture are fructooligosaccharide (FOS), transgalactooligosaccharide (TOS), inulin, glucooligosaccharide, xylooligosaccharide, isomaltooligosaccharide, soybeanoligosaccharide, polydextrose and lactosucrose. Natural sources of prebiotics in vertebrates include chicory, onion, garlic, leek, tomato, honey, etc.

Immunostimulants: Use of antibiotics and chemotherapeutics has negative impacts such as immunosuppression, development of resistance and bioaccumulation in the tissues and environment.

Hence, strengthening the defence mechanism of fish and shrimp through prophylactic administration of plant based immunostimulants is considered as a promising alternative. Natural plant products with active principles such as alkaloids, flavanoids, pigments, phenolics, terpenoids, steroids, and essential oils are identified for modulation of the innate immune response by anti-stress, growth promotion, appetizer, immunostimulation, aphrodisiac and antimicrobial properties in fish and shrimp. But, the lack of scientific mechanism of action and standardization hamper the wide acceptance of herbal immunostimulants not only in aquaculture but also in veterinary and human medicine.

Essential oils: Essential oils (EOs) are natural volatile liquid fractions from plants that are generally recognized as safe substances having antibacterial, antiviral, antifungal, and insecticidal activities. Due to their antimicrobial properties, these oils may constitute alternative prophylactic and therapeutic agents in aquaculture. They are obtained from flowers, buds, seeds, leaves, twigs, bark, herbs, wood, fruits and/or roots. The primary roles of essential oils in plants are believed to be as pollinator attractors and defenses against pathogens and pests. The essential oils of many plants contain phenolic compounds, and these comprise the majority of plant antimicrobial components. Among the most studied are thymol from thyme and oregano; cinnamaldehyde from cinnamon; eugenol from clove, carvacrol from oregano and anethole from anise, whose antibacterial properties have been examined in several studies.

Phage therapy: Phage therapy has gained much attention for its advantages in preventing and controlling infections in aquaculture. Bacteriophages are defined as viruses that can infect, multiply and kill susceptible bacteria. They are both ubiquitous and abundant in the environment, especially in seawater. Phages have been studied for their therapeutic properties and ability to control infectious bacteria. However these studies were later abandoned due to the introduction of cheap broad-spectrum antibiotics. Recently, after the increase in bacterial antibiotic resistance, phage therapy has gained its importance as an effective alternative to antibiotics.

Targeting increased aquaculture production by intensive aquaculture poses threats due to disease outbreaks, which signify the need of therapeutics. At the same time, the therapeutics should be of environmentally friendly. Since antibiotic resistance threatens the use of antibiotics in aquaculture, effective alternatives are critically important for aquaculture. Hence, researches on therapeutic and prophylactic use of managemental aspects, vaccines, probiotics, prebiotics, immunostimulants, EOs and phage therapies in aquaculture is need of the hour.

BIODYNAMIC PREPARATIONS IS AN ALTERNATIVE FOR ANTIBIOTICS IN FOOD PRODUCTION

M. Sakthivel

Hatsun Agro Products Limited, Chennai-600 067

Following the discovery of penicillin, Alexander Fleming warned about the possible development of resistance if antibiotics are not used cautiously. Antibiotics are widely using in human medicine for treatment of infectious disease and in animal husbandry and agriculture for improved productivity. Use of antibiotics as growth promoter is considered as the primary cause for development of antibiotic resistant bacteria. To minimize the use of antibiotics in agriculture several alternative biocontrol agents have been suggested. Biodynamic farming is one such approach which has the potential to enhance the productivity in food crops, dairy, poultry and aquaculture. Biodynamic farming is based on the knowledge that the soil, plants, animals and farmers work together in one agricultural cycle. Biodynamic products are included in the list of materials and techniques permitted in organic farming by European community (EC) regulation. The biodynamic products prepared by mixture of five products originating from cow contain macro- and micro-nutrients, amino acids, and growth promoting substances like indole acetic acid, gibberellins and beneficial microorganisms. Presence of naturally occurring beneficial microorganisms, predominantly bacteria, yeast, actinomycetes, and certain fungi will function to enhance the natural productivity in the soil and water. In agriculture the biodynamic products are used as an organic fertilizer for enhancing soil fertility, source of fuel, for dressing seeds, plastering cut ends of vegetatively propagated sugarcane, dressing plant wounds etc. These products have immense potential to be used in aquaculture to enhance the natural productivity and improve the health of culture pond environment.

SPEAKERS

Dr K. K. Vijayan

Central Institute of Brackishwater Aquaculture (CIBA), Chennai

Renowned fisheries scientist Dr.Vijayan before becoming director of CIBA, served as Head of the Marine Biotechnology Division, CMFRI, Kochi. With post doctoral research in University of Mississippi, USA and University of Liege, Belgium, Dr.Vijayan has more than two decades of research experience in aquatic health management including development of molecular tools for diagnosis of economically important diseases of marine organisms. For the first time in the country he has commercialized diagnostic kit for white spot syndrome virus which was helpful in reducing the cost of diagnosis to the stakeholders. He played important role in development and commercialisation of one of the important nutraceuticals, the CadalminTM GMe (Green Mussel Extract) from marine origin. His current interests are addressing issues related to antibiotic residues in aquaculture products and development of alternative strategies. He has several research papers in national and international journals, book chapters, patents and commercial release of products to his credit.

With additional responsibility as Member Secretory Coastal Aquaculture Authority (CAA), Dr.Vijayan is leading the R&D and regulatory measures for increasing the fishery production through economically viable, environmentally sustainable and socially acceptable approach.

P.K. Patil

Central Institute of Brackishwater Aquaculture (CIBA), Chennai

Veterinarian by profession Dr.Patil is presently working as Project Coordinator for an ICAR funded project "All India Network Project on Fish Health", this is a collaborative project involving 10 research institutes working in the area of aquaculture and fisheries in India. Under the project drugs used in aquaculture have been documented and categorised from all the states including north eastern region and J&K. He is actively involved in developing standards for scientific use of drugs in aquaculture and establishing withdrawal periods and assessing the impact on the environment. Dr.Patil has industry collaborative projects with Seafood Exporters Association of India (SEAI), Chennai, Rajshree Biosolutions Pvt. Ltd., Theni, Tamil Nadu, Hatsun Agro Pvt. Ltd., Chennai, Neer Aqua Pvt. Ltd. Navsari, Gujarat and Revelations Biotech Pvt. Ltd., Hyderabad. His work is mainly focused on development of natural products, probiotics and vaccines for use in aquaculture which help in disease prevention and reduce the dependence on drugs especially antibiotics. He has waste experience in working with developmental agencies, academics, industry and research in the areas of animal husbandry, poultry and aquaculture.

Dr. S.V. Alavandi

Central Institute of Brackishwater Aquaculture, ICAR, Chennai.

Doctorate in Microbiology from University of Madras, has 26 years experience in the field of aquatic Microbilogy. He has published 54 research articles and worked as a principal Investigator for several projects from DBT, DST and NBAIM. He has guided four Ph.D., students. His major fields of research are Bioremediation in aquaculture, Probiotics in aquaculture, Virulence of Vibrio harveyi, Phage therapy, shrimp disease diagnosis and prevention and viral metagenomics.

Dr. Sujith J Chandy

Christian Medical College, Vellore, Tamil Nadu

National expert in clinical trials ethics, pharmacovigilance, pharmacoepidemiology and medical education. His key publications have been in the area of antibiotic use. Dr. Chandy has played a significant role as resource person in antibiotic use and stewardship at regional and national workshops, Karolinska Institute and University of Dundee/BSAC MOOC training programme, coordinator for the Antibiotic Stewardship and Prevention of Infection Control programme (ASPIC), observer in AMR STAG meetings at WHO and as Head, ReAct Asia Pacific. Dr. Chandy's interests include clinical pharmacology, medicine use and safety, and pharmaceutical ethics. However his passion continues to be speaking about antibiotic use and stewardship to students, professionals and the wider community.

Dr. R. N. Bhaskar

University of Agricultural Sciences, GKVK Bangalore

Contributed significantly in the field of Sericulture and Seri agro ecosystem, Dr. Bhaskar has worked on Nutritional management in mulberry under rainfed condition and use of medicinal plants against fungal, bacterial, viral and protozoan diseases of silkworm, *Bombyx mori*. The beneficial effects have been tried on different instars of silkworm. Recipient of Dr. B.R. Ambedkar award from Hoechst India Limited 1996, Rashtriya Gaurav Award by India International Friendship Society 2010 and Outstanding International Teacher by Srishti International Colombo, Sri Lanka 2015 and certificate of appreciation by ZOOLOGICAL SOCIETY OF INDIA during 2007. He has published more than 90 research articles in reputed National and International journals. He has written three books and handled 4 research projects financed by U.G.C. and RKVY, GOI. He has successfully guided four Ph. D. and nineteen M.Sc. (Agri) Sericulture degree students.

Dr. Padma Krishnan

Institute of Basic Medical Sciences, University of Madras, Chennai

Doctorate in Medical Microbiology from University of Madras, has extensive research experience in reputed institutes like Haffkine Institute, Mumbai and Foundation for Medical Research, Mumbai. With 25 years of experience in the field of Microbiology. She has published several research papers and worked as Principal Investigator for several projects from UGC, ICMR-Indo-German research project, Ranbaxy, Nicholas Piramal and Reddy's Laboratories. She has been conferred Fellow of the Association of Biomedical Scientists (FABMS) title and recipient of several national and international travel grants for presenting at international conferences in USA, UK, France and Germany. Her major fields of research are Characterization of antibiotic resistance and virulence determinants among Staphylococcal and Enterobacterial isolates of human, animal and environmental origin.

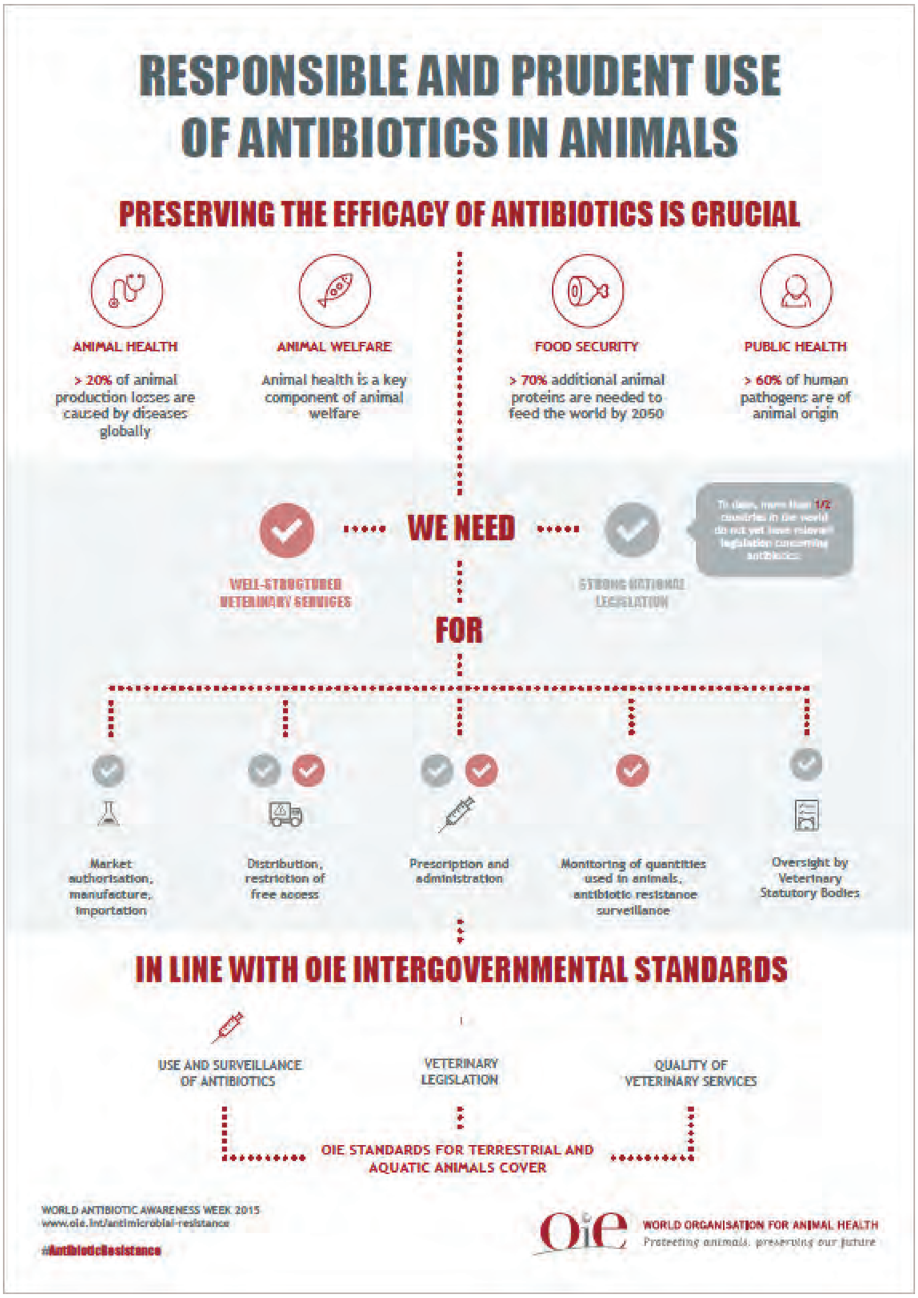
Dr. S. Ramesh

Tamil Nadu University of Veterinary and Animal Sciences, Chennai

Specialized in Veterinary Pharmacology and Toxicology, Dr. Ramesh has served for two decades as a teacher for graduate and post graduate studies. Specialized pharmacokinetics of antimicrobials in poultry and goats he has deduced the dosage of many antibacterial drugs in poultry and goats. He has standardized HPLC assay methods for different antimicrobials and has worked on the status of resistance in bacterial isolates from milk and poultry. He has completed four research projects and is currently the PI of ICAR Outreach programme on 'Monitoring of drug residues and environmental pollutants'. He has published several research papers and has authored chapter in a book on mastitis. In his present position, he is organizing the Certificate Course in Laboratory Animal Sciences, the only course accredited by Federation of European Laboratory Animal Scientists Associations (FELASA), outside Europe.

V. Paranidharan

Doctorate in Plant Pathology worked McGill University, CANADA for identification of primary and secondary resistance related biomarkers and mycotoxin (DON) by GC/MS-Quadrupole, GC/MS-TOF and GC/MS-ion-Trap, identification and quantification of mycotoxin metabolites by SATURN, MassLynx, AMDIS and MET-IDEA softwares and identification of deoxynivalenol and their derivatives in wheat by GC/MS. Undergone trainings in Texas A&M University, USA and Bari, Italy to understand the function of the lipoxygenase genes in maize for aflatoxin management and fusarium. He has completed several research projects and published papers in national and international journals. He teaches plant pathology and crop protection courses to postgraduate and doctoral students at TNAU, Coimbatore.


RESPONSIBLE AND PRUDENT USE OF ANTIBIOTICS IN ANIMALS
PRESERVING THE EFFICACY OF ANTIBIOTICS IS CRUCIAL
ANIMAL HEALTH
> 20% of animal production losses are caused by diseases globally
ANIMAL WELFARE
Animal health is a key component of animal welfare
FOOD SECURITY
> 70% additional animal proteins are needed to feed the world by 2050
PUBLIC HEALTH
> 60% of human pathogens are of animal origin
WE NEED
WELL-STRUCTURED VETERINARY SERVICES
STRONG NATIONAL LEGISLATION
FOR
Market authorisation, manufacture, importation
Distribution, restriction of free access
Prescription and administration
Monitoring of quantities used in animals, antibiotic resistance surveillance
Oversight by Veterinary Statutory Bodies
IN LINE WITH OIE INTERGOVERNMENTAL STANDARDS
USE AND SURVEILLANCE OF ANTIBIOTICS
VETERINARY LEGISLATION
QUALITY OF VETERINARY SERVICES
OIE STANDARDS FOR TERRESTRIAL AND AQUATIC ANIMALS COVER
WORLD ANTIBIOTIC AWARENESS WEEK 2015
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Protecting animals, preserving our future

FIGHTING ANTIBIOTIC RESISTANCE

HANDLE ANTIBIOTICS WITH CARE

Antibiotics are essential resources for human health, animal health and animal welfare. Their misuse can result in the emergence of bacteria resistant to their action, also called antibioresistant. This phenomenon deeply threatens the control of diseases worldwide.

We need to collectively ensure the responsible and prudent use of antibiotics in animals to preserve their effectiveness.

WHAT CAN YOU DO AS FARMERS ?

1. Only use antibiotics when prescribed or administered by a veterinarian
2. Follow the recommended dosage and length of treatment even if your animal seems to have recovered
3. Exclusively buy antibiotics from authorised sources
4. Vaccinate and institute good hygiene and husbandry practices to prevent infections
5. Keep adequate written records of all antibiotics used as well as the laboratory results

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#AntibioticResistance

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World Health Organization

*modified from source

FIGHTING ANTIBIOTIC RESISTANCE

HANDLE ANTIBIOTICS WITH CARE

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We need to collectively ensure the responsible and prudent use of antibiotics in animals to preserve their effectiveness.

WHAT CAN YOU DO AS POLICY MAKERS?

1. Control the use of antibiotics through supervision of well-trained veterinarians
2. Prevent the circulation of non-quality products
3. Encourage research on alternative treatments to antibiotics
4. Ensure that appropriate legislation supports Veterinary Services
5. Raise awareness on the responsible and prudent use of antibiotics in animals based on OIE standards

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World Health Organization


ANTIBIOTIC RESISTANCE
WHAT THE AGRICULTURE SECTOR CAN DO
HANDLE ANTIBIOTICS WITH CARE
Antibiotic resistance happens when bacteria change and become resistant to the antibiotics used to treat the infections they cause.
1 Ensure that antibiotics given to animals—including food-producing and companion animals—are only used to control or treat infectious diseases and under veterinary supervision
2 Vaccinate animals to reduce the need for antibiotics and develop alternatives to the use of antibiotics in plants
3 Promote and apply good practices at all steps of production and processing of foods from animal and plant sources
4 Adopt sustainable systems with improved hygiene, biosecurity and stress-free handling of animals
5 Implement international standards for the responsible use of antibiotics and guidelines, set out by OIE, FAO and WHO
www.who.int/drugresistance
www.oie.int/antimicrobial-resistance
www.fao.org/antimicrobial-resistance
#AntibioticResistance
Food and Agriculture Organization of the United Nations
OIE WORLD ORGANISATION FOR ANIMAL HEALTH
World Health Organization

#AntibioticResistance

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AQUATIC ANIMAL HEALTH AND ENVIRONMENT DIVISION

ICAR-Central Institute of Brackishwater Aquaculture (CIBA)
#75, Santhome High Road, R.A. Puram, Chennai, Tamil Nadu. 600 028

Research on brackishwater aquatic animal health and environment was initiated at the Central Institute of Brackishwater Aquaculture since 1990. Since then it has grown in terms of expertise, manpower and facilities. The Aquatic Animal Health and Environment Division or the AAHED in short, has scientists with all relevant specialities and expertise in Microbiology, Virology, Pathology, Parasitology, Biotechnology, Molecular Diagnostics, Soil and water Chemistry, Environment and Aquaculture. The AAHED has well established laboratory facilities for carrying out cutting edge research in molecular biology in addition to aquatic animal health and environment management including diagnostics, prophylactics and health management in brackishwater aquaculture. The advanced facilities have been developed with funding support from ICAR, National Agricultural Research Project (NARP), World Bank, National Agricultural Technology Project (NATP), All India Network Project on Fish health (AINP), Consortia Research Platform on Diagnostics and Vaccines (CRP-D&V), National Innovations in Climate Resilient Agriculture (NICRA) project, Department of Biotechnology and National Fisheries Development Board with dedicated efforts of scientists. A well designed wet lab is also in place for carrying out live aquatic animal experiments and evaluating Koch's and River's postulates.

The AAHED, CIBA has the mandate to carry out research on (a) economically impacting diseases of brackishwater culture species and develop technologies for rapid diagnosis, prophylaxis and control; (b) brackishwater environment and develop mitigatory measures as required; and (c) provide technical and policy support to the Government on matters pertaining to aquatic animal health and environment management to improve aquaculture productivity.

The AAHED of CIBA was the first to commercialise a white spot syndrome diagnostic kit to a premier Biotechnology company in the year 2002. AAHED has the expertise and capacity to carry out all the proposed levels of Diagnostics of OIE listed brackishwater pathogens, and has been serving as a National Referral Laboratory to the Department of Animal Husbandry Dairying and Fisheries, Ministry of Agriculture and Farmers' Welfare, Govt. of India.

The environment section of AAHED has the expertise to look into all aspects of abiotic parameters. Novel methods have been developed for the bioremediation and environmental monitoring of the brackishwater rearing systems, including hatcheries and grow-out farms. The section has developed climate smart solutions such as carrying capacity assessment tools for optimisation of brackishwater aquaculture development. The unit has expertise in climate related matters and capacity for environmental impact assessment. AAHED, CIBA has been carrying out research on various aspects of prophylactics and therapeutics of brackishwater aquatic animal diseases and has published over 60 research publications in peer reviewed national and international journals, produced 15 Ph.Ds, who are currently employed in key positions in various Institutions in India and abroad.

Aquaculture, Biotechnology & Molecular Diagnostics : Dr. K.K. Vijayan, Dr. S.K. Otta, Dr. Satheesha Avunje

Microbiology & Virology : Dr. S.V. Alavandi, Dr M. Poornima, Dr. P. K. Patil, Dr. Sanjoy Das, Dr. Sujeet Kumar, Dr. T. Bhuvaneshwari, Dr. N. Lalitha

Parasitology & Pathology : Dr. K. P. Jithendran, Dr. Ezhil Praveena, Dr. R. Ananda Raja, Mr. T. Sathish Kumar, Dr. Vidya Rajendran

Soil & Water Chemistry : Dr. M. Muralidhar, Dr. R. Saraswathi, Mr. P. Kumararaja, Ms. C. Suvana

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