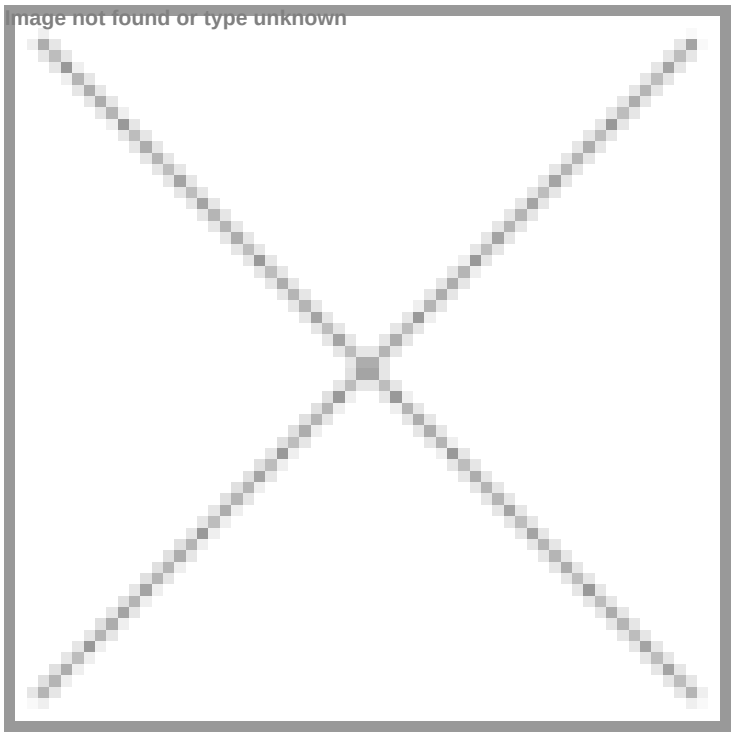
BioSpectrum the business of Bio & Health Sciences

"India must leverage its rich resources to establish phage libraries and cocktails"

30 January 2024 | Views | By Anusha Ashwin

India houses a wide spectrum of bacteriophages that can be isolated and used in the treatment of antimicrobial resistance (AMR), in agriculture as a microbicide and in several other ways where pathogenic bacteria need to be removed. The country has taken cognizance of its benefits in the last few years and is now taking decisions to support the research on bacteriophages. However, the argument remains that there is not enough being done. Sharing some unknown facts and information about the application of bacteriophages and the associated regulatory requirements, Founder & CEO of MicroGO, Rachna Dave and Dr Hiren Joshi, Scientific Officer, Bhabha Atomic Research Centre, Kalpakkam, co-respond to a few questions posed by BioSpectrum India.



How is research in India contributing to the development of novel bacteriophage-based technologies, such as phage engineering or phage cocktails?

In India, a substantial number of laboratories are actively engaged in bacteriophage research. The pioneering efforts of Dr Chhiber, Dr Gopal Nath, Dr Urmi Bajpai, and others have laid a robust foundation for bacteriophage-related studies. Presently, more than 20 to 30 research facilities across the country are dedicated to isolating and characterising bacteriophages, with a specific focus on combating pathogens prioritised by the Indian Council of Medical Research (ICMR).

Notably, the Bhabha Atomic Research Centre (BARC) has recently announced the establishment of a Phage Bank. This Phage Bank houses fully characterised bacteriophages and cocktails tailored for targeting all ICMR listed priority pathogens.

While bacteriophage engineering is an emerging field in India, it is essential to highlight that substantial progress has been

made in the study of endolysins. These enzymes, produced by phages, play a critical role in creating breaches in bacterial cell walls. Many research laboratories in India have successfully developed enhanced variants of endolysins with improved activity.

What is the current market size of bacteriophage-based products and therapies in India, and how is it projected to grow in the coming years?

Estimating the market size of bacteriophage-based products in India presents a challenge due to their vast potential applications, ranging from phage therapy to aquaculture, poultry, and plant protection. Nevertheless, based on various estimates, it is projected to reach approximately $50 million by the year 2030. This growth is further substantiated by recent developments, such as the establishment of a new production facility in Nasik by Proteom Biotech, a Polish company. Additionally, several other companies are currently in the process of setting up pilot-scale plants for bacteriophage production, underscoring the increasing interest and investment in this promising field.

Bacteriophages have shown significant promise in tackling Antimicrobial Resistance (AMR) due to their ability to target and kill specific bacterial strains. Please elaborate on this statement and also share some examples from India-based success stories of AMR tackling phages and also add a note on its effectiveness compared to traditional antibiotics?

AMR is indeed a far more significant and pressing issue than it might initially appear, primarily due to underreporting. According to estimations, the toll of AMR could result in more than 10 million deaths by 2023. This looming crisis is exacerbated by the extremely limited availability of new antibiotics in the market, making it an incredibly challenging problem to address.

In this dire context, bacteriophages are emerging as one of the most promising solutions to combat AMR infections. With the scarcity of effective antibiotics, bacteriophages offer a viable alternative. In India, there have been approximately 200 patients successfully treated with phage therapy, boasting an impressive success rate exceeding 80%. This number is steadily increasing as more clinicians and infection prevention specialists embrace this innovative technology. The adoption of bacteriophages holds significant promise in the fight against the growing threat of AMR.

Are there any unique indigenous bacteriophage strains or resources in India that offer a competitive advantage or research opportunities?

Yes, India being highly populous country and various other factors do play a role in the bacterial diversity found in our wastewaters, hospitals waste waters and other environmental samples. This unique environment presents an exceptional opportunity to isolate a wide range of divergent bacteriophages. These bacteriophages can exhibit specificity towards various pathogens, making India an ideal setting for their discovery.

It is imperative to leverage this rich resource to establish comprehensive phage libraries and cocktails. These collections can prove highly effective against a broad spectrum of bacterial infections. By tapping into the wealth of bacteriophages in India's diverse microbial ecosystems, we can potentially develop innovative solutions for combating infectious diseases and antimicrobial resistance on a global scale. This approach holds great promise for the future of healthcare and pathogen control.

What is the regulatory landscape for bacteriophage-based therapies and products in India, and how is it evolving to accommodate this emerging field?

The regulatory framework for bacteriophages and phage therapy is currently in its early stages of development in India. However, it is widely recognised that bacteriophages are a natural part of the human microbiome, and as such, they typically do not elicit significant immune responses or other adverse effects. This understanding aligns with the principles outlined in the Helsinki Declaration.

Under the Helsinki Declaration, bacteriophages or phage therapy can be administered to patients on compassionate grounds.

The primary requirements include certification from two treating clinicians and informed consent from the patient. This approach acknowledges the urgency and need for innovative treatments, particularly when conventional antibiotics may not be effective.

Furthermore, the ICMR is actively engaged in shaping the regulatory framework for bacteriophages. Researchers are encouraged to provide additional data and insights to contribute to the development of a more comprehensive regulatory framework. This collaborative effort underscores the commitment to advancing phage therapy as a viable option for addressing infectious diseases and antimicrobial resistance in India.

What are the challenges and limitations of using bacteriophages in India, such as issues related to production, purification, stability, and delivery methods?

The primary challenge lies in the realm of regulation. The absence of clear guidelines has led to hesitancy among clinicians to adopt this approach. Moreover, India currently lacks a dedicated phage bank or repository where fully characterised, ready-to-use bacteriophages are stored. Establishing such a repository is pivotal in making phage therapy a viable alternative.

Interestingly, institutions like the BARC are taking steps to fill this gap. They are in the process of establishing a Phage Bank, housing fully characterised bacteriophages and phage cocktails, ready for deployment. Furthermore, efforts are underway to set up production facilities capable of culturing up to 10 liters of bacteriophages. Nevertheless, the pressing need is for universally applicable protocols and production guidelines that can be uniformly implemented across all production facilities.

Can you share some information on the ongoing clinical trials or research projects related to bacteriophages in India, and what are their objectives and outcomes?

Vitalis Phage, Delhi collaborates with numerous hospitals and clinicians in the practice of phage therapy, not as part of formal clinical trials. To the best of my knowledge, Dr Gopal Nath at Banaras Hindu University (BHU) has conducted several clinical trials, primarily focused on chronic wounds such as diabetic foot ulcers and trauma wounds resulting from road accidents. The results of these trials have been highly promising.

What is the level of public awareness and acceptance of bacteriophages as an alternative to antibiotics in India, and are there any public health campaigns promoting their use?

Awareness of phage therapy remains relatively low, even among clinicians who are only beginning to familiarise themselves with this innovative approach to infection treatment. However, recent conferences like International Conference on Bacteriophage Research and Antimicrobial Resistance (ICBRAR-2023) have played a pivotal role in disseminating information about phage therapy. As a result, an increasing number of clinicians are showing interest in adopting this alternative therapy.

Nevertheless, significant challenges persist. Availability of comprehensive clinical data and the production of phages in laboratories compliant with Good Manufacturing Practices (GMP) standards are key bottlenecks. Addressing these challenges is essential to further advancing the adoption of phage therapy and ensuring its effectiveness and safety in clinical settings. The combination of increased awareness and improved infrastructure can pave the way for more widespread and successful implementation of phage therapy in healthcare.

What are the funding and investment trends in the Indian bacteriophage sector, and are there any notable collaborations between academia, industry, and government agencies?

While not yet widely prominent, there are indeed a few companies and research institutions that are making extensive strides in the field of phage therapy. For instance, Vitalis Phage has established collaborations with prestigious institutions like the Eliava Institute in Georgia, a globally renowned centre for phage therapy. In India, laboratories at institutions such as BHU (Banaras Hindu University), Panjab University, and research organisations like BARC are actively engaged in phage research, accumulating significant expertise in the field.

The increasing visibility and significance of phage research suggest a growing interest and investment in this field in the coming years. As awareness and research efforts continue to expand, it is likely that phage therapy will become an even more prominent and promising approach in the fight against infectious diseases and antimicrobial resistance.

How do Indian researchers and companies compare internationally in terms of bacteriophage research and development?

The growth and interest in phage research are becoming increasingly evident. Historically, there were only a handful of researchers dedicated to this field. However, the recent ICBRAR-2023 conference, which attracted around 300 researchers, signifies a notable shift. The attendance of such a significant number of participants demonstrates that the trend in phage research is on the rise.

Moreover, the emergence of many young investigators getting involved in phage research suggests a promising future for the field. It appears that phage research is entering an exponential phase of growth, driven by the enthusiasm and contributions of both seasoned researchers and the next generation of scientists. This bodes well for the continued development and application of phage therapy and its potential to address critical healthcare challenges related to infectious diseases and antibiotic resistance.

What intellectual property and patent trends are associated with bacteriophage-related innovations in India?

Bacteriophages are natural entities, and this poses certain limitations when it comes to obtaining intellectual property (IP) protection for them. To the best of my knowledge, there haven't been specific patents granted for phages in recent times. However, researchers in the field of phage therapy and phage-related processes can explore opportunities for process patents. Process patents may cover various aspects of phage research and application, including methods of isolation, purification, characterization, and manufacturing. Additionally, processes related to the formulation and delivery of phage therapies could be considered for patent protection. While the genetic material of phages themselves may not be eligible for patenting, the innovative methods and processes developed in the course of phage research can potentially be protected.

Anusha Ashwin

Click here to read the next story on bacteriophages