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Virome against Enteropathogens Present in Ganges Water

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The Ganges is home to a high variety of microorganisms, both beneficial and harmful. Anthropogenic activities cause depletion in microbial communities at urban sites of river Ganga. From the ancient period, it is believed that purification of Ganges Water does not possible after long storage and so it can be used frequently for cooking, drinking, or bathing purposes. About 200 years ago, British colonial scientists suggested that Ganga may contain unique microbial life, which makes it relatively more resilient to putrefaction. That unique microbial life is the virome. The presence of various kinds of viruses gives Ganga its self-purificatory property.

Keywords: Bacteriome-Virome-Human Host Interaction; Ganga, Virome; Human Gut; Self-purification; Virus-Mediated River Cleansing.

The Ganges water has been consumed from time immemorial for domestic as well as remedial purposes. It is well known that, over the years, the Ganga water has become inadequate and unsafe for drinking. The Ganga River is home to a large population of pathogenic bacterial species. But still, the river water continues to be used for domestic purposes and, surprisingly, the effects are not as deadly as expected. The reason behind this peculiarity is expected to be the presence of virome in the river Ganga. This review revolves around the interaction of virome present in the Ganges with the pathogenic bacteriome and with the river water consumers. It aims at highlighting the mechanisms involved in the protective roles played by virome against severe waterborne diseases. It further aims to present a few findings that propose that Ganges Water contributes novel antimicrobial aspects which have the possibility to deliver a need basis for the progress of novel antibacterial components in near future.

Outreaches of Ganga

Ganga is the great river of the plains of the northern Indian subcontinent. The Ganga River originates from the confluence of the Bhagirathi and Alaknanda at Devaprayag town of Uttarakhand. The Alaknanda River emerges from the foot of Gangotri Glacier at Gomukh in the western Himalayas. It drains one-fourth of the Indian Territory and finally drains into the Sunderbans delta in the Bay of Bengal (Fig 1).

The Present Condition of the River Ganga

The ever-increasing population and urbanization in the river basin is leading to organic carbon buildup and high environmental deposition. The DO level of the river water

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depletes substantially due to tannery effluents[1]. Increased BOD values (e"5.2ppm) [2] are for the straight flow of sewage material in the river and the establishment of a large number of apartments, industries, and hospitals on the river banks [3] making its water unfit for drinking and refreshment.

The river water remains highly contaminated through sewage and tannery effluents are treated [4]. Ganga has high coliform contamination (5–20 times more than the tolerable limit) and high Cultivable Vibrios Count mainly for the direct flow of sewage and open removal around the banks of the river. Due to this reason, the annual periodic diarrheal recurrences in monsoon and post-monsoon seasons in South Bengal are initiated. The microbial and chemical contamination are caused mainly by rapid industrialization and urbanization throughout the river banks which impose an immense threat to human health[5].

The Major Causes of Pollution in Ganga

A large amount of untreated waste disposal in the Ganges is due to the lack of functional treatment plants. 6.7% of cities and towns have limited sewage treatment and 0.25% have complete sewage treatment[6] (Fig 2), of which most are primarily useless because of lack of functionality by construction and upkeep, absence of workforce, poor management, and deficiency of constant electricity [7]. Feces in open areas can make their way into streams easily and overflows causing contamination of nutrition sources[8]. Almost 1 billion liters of untreated sewage are dumped in the river daily which has doubled in the last 20 years and another 100% increase in the next 20 years is predicted[9].

Pristine Nature of the Ganges

Ganga Vs Other Indian Rivers

A study established that the river Ganga is the most pristine of all the Indian rivers[6]. Although the presence of pathogens, heavy metals, and other toxicities are higher in Ganga as compared to other rivers, still Ganga retains its purity due to the fact that it contains a great number of bacteriophages as compared to Narmada and Yamuna[2].

Self-Purificatory Aspects of Ganga

So far this review has discussed about the level of contamination in the Ganges, the major causes of pollution in the river and how these factors contribute to make Ganges a severe threat to our health. High amounts of Enteropathogens are deposited in Ganges having high potential to cause fatal health issues in children and adults residing in the banks of the Ganges, children being at higher risk than adults. So, a very high rate of disease occurrence and infectivity is expected to result from the consumption of Ganga water.

However, the reality is different. In the past it was proven that the Ganges retains a self-purifying capacity[2] that is derived from its inquisitively high capacity to maintain dissolved

Fig. 1. Map showing the flow of Ganga

oxygen[10]. Lack of suitable DO leads to infected condition and causes increases BOD in the river[9]. The maintenance of high DO levels is performed by specific bacteriophages which feed on certain bacterial population of the river, thus lowering its pathogenic load.

The Call for the Use of Virome against Enteropathogens of Ganges

Several studies have shown that the Ganges exhibit much higher levels of Bacteriophages than any other river of the country which correlates with the self-purificatory properties of Ganga. Bacteriophages being able to lyse the bacterial cells and affect their population seem to have a very significant role in lowering the level of contaminants in the Ganges and bringing down the risk of serious health hazards. *E. coli* is a desired indicator for freshwater recreation. It's presence gives straight evidence of fecal contamination from warm-blooded animals. The anti-microbial agent resistance profile provides the evidence that river Ganga is a source of multiple-antimicrobial-resistant *E.coli*[11]. *E.coli* isolates from urban areas have resistance to more antibiotics than rural isolates possibly due to greater contact to antibiotics. *E. coli* may transfer between virulent and non-virulent making these forms indistinguishable from normal gut flora[12].

A study on Multi-Drug Resistant Bacteria in the Ganga surface waters of Kolkata detected Superbugs which are resistant to multiple drugs[13]. More than 2000 tons antibiotics are made these days and MDR bacteria are maximum at the industry sites and its adjacent river. In *Escherichia coli* and *Pseudomonas aeruginosa,* many drug efflux genes are assembled which resemble the ABC transporter genes[14] (Fig 3).

The severity of heavy metal contamination can be indicated very well by the presence of the microbial community[15]. The lower and middle

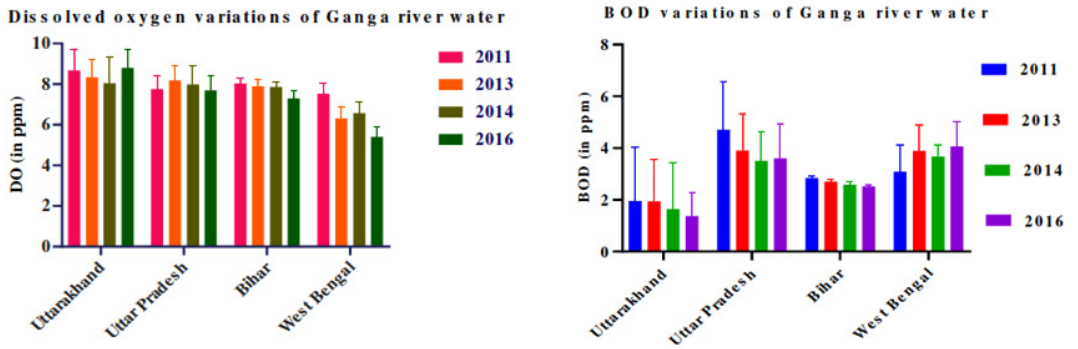

Fig. 2. Variations in Dissolved Oxygen Levels and Biological Oxygen Demands Over The Years From 2011 to 2016[5]

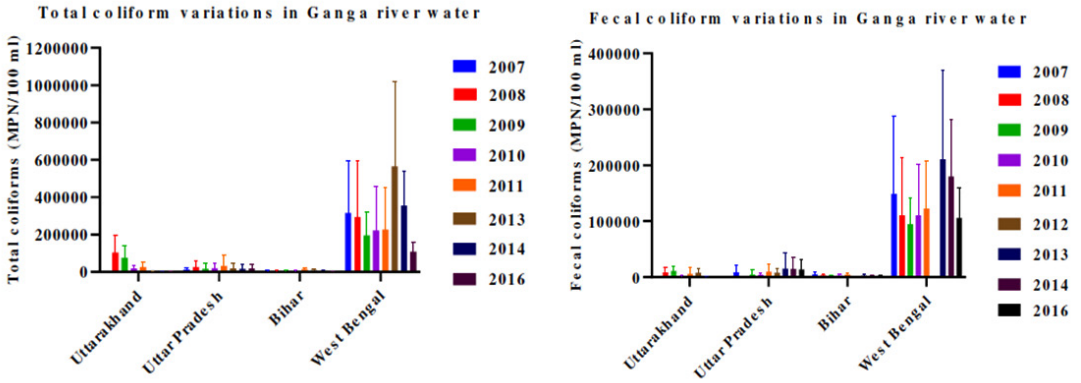

Fig. 3. Total Coliform and Fecal Coliform Variations in Ganga Over The Years From 2007 to 2016[5]

stretches of Ganga have high microbial and heavy metal contamination[16]. Further, some bacterial species which are available in Ganga water, like *Bacillus cereus*, *B. thuringiensis* and *B. subtilis*, are identified to reduce hexavalent chromium (CrVI), a toxic and carcinogenic form, to the non-toxic trivalent chromium (CrIII)[17]. This again indicates the curative properties of Ganges because CrIII is a necessary nutrient that stimulates metabolism of glucose, fat and protein by helping the activity of insulin in humans and animals[18]. Ganga reveals certain distinct qualities of higher alkalinity and pH and presence of trace elements. These have a role in self-purificatory properties of river Ganga by influencing the growth of bacteriophages. Phages usually need divalent metal ions for their growth, again their stability, attaching to the host cell for the entry of their nucleic acid and multiplication all are controlled by the ions[19].

All these evidences call for study about the implications of virome. Virome seems to have strong contribution in the curative properties of Ganga water.

Why to Rely on Virome?

Several types of purifying activities have been adopted to have a pathogen-free Ganga, but none have been proved to be effective enough. However, a natural purification mechanism has been observed in the Ganges in several studies time and again. Some of which are listed below.

• In 1896, Ernest Hankin found phages that thrived in tap water, died in non-boiled but filtered Ganges water and also died in boiled Ganges water[20].

• In 1916, Felix d'Herelle identified factors which are heat labile and difficult to filter but exhibit antimicrobial activity[21].

• IIT Roorkee in 2019, isolated Superphage from Ganga, decoded lysine gene and cloned lysine protein with great potential as antibacterial pharmaceutical [22].

• CSIR identified >20 types of phages in Ganges that fight microbes which cause TB, pneumonia, cholera etc[23].

Nature and Components of the Human Gut Virome

The human gut virome is usually individual specific and can be stable for one year. A persistent personal virome usually present in the most stable fraction of viruses of any individual and that can be linked to highly predominant gut bacterial taxa[24].

Effect of Gut Virome in Homeostasis and Dysbiosis

The mammalian intestinal virome usually consist of viruses which can multiply in both eukaryotic and prokaryotic cells. The virome activates a mutual relationship with eukaryotes or prokaryotes. It contribute to intestinal homeostasis after inducing host immunity and microbial ecology. The pathogenesis of some diseases via microbial host lysis may lead to dysbiosis and that can be contributed by the virome[25].

Many bacterial species inhabiting our Gastro-Intestinal track are beneficial for us which maintain a quite stable population in the human gut, the normal microbiota of our gut. However, this normal microflora gets imbalanced under certain cases, like during the course of antibiotics which is prevented by the human gut virome. Viruses provide antibiotic resistance via Horizontal Gene Transfer (HGT). HGT also leads to the occurrence of virulence in the bacterial species which triggers immune response in the host generating Reactive Oxygen Species, which in turn triggers more HGT. Antibiotics also cause induction of prophage and lysis of commensals resulting in pathogenic bacterial species to invade the host tissues due to elimination of competition. So, a supplement for use of antibiotic is necessary, which is provided by Phage Therapy. Phage Therapy can be administered to kill pathogens. Latent viral infection causes immune activation and prevents pathogenic infection and removal of pathogens. Thus a Phage-Mediated Immunity is generated[26].

Thus, interactions of viruses with the host immune system as well as the commensal bacteriome of the host are both positively and negatively regulated[27]. More studies will reveal the proper mechanisms of these interactions and how these interactions can be directed for the advent of human utility.

The functional role of viruses in humans and animals is not known clearly till date. One hypothesis concludes that few of these viruses influence on human health indirectly by eradicating viral pathogens through viral intervention or by cross-immunity[28]. It has been revealed that patients with HIV and hepatitis G virus interrupt

the manifestation of AIDS[29]. Though, few viruses proliferate the risk of secondary infection by an analogous virulent genotype or new microbial/ viral agents by maintaining chronic inflammation or stimulating virus-related carcinogenesis in particulars with a particular immunological disorder[30]. Different agents of the *Papillomaviridae*, *Polyomaviridae,* and *Herpesviridae* families have been associated with cancers in humans.[31,32,33,34].

So, it can be concluded that interactions of viruses with humans go after simple parasitism. Several eukaryotic viruses can have persistent interactions with their counterpart. The beneficial or adverse effects of such interactions may be determined by the structural site of infection, the genotype of host or immune status, or the existence of other microbes and Viruses.

Methods of detection of Viruses or VLPs from the Ganges

Now that such a huge level of viral utility is estimated to be already occurring naturally in the Ganges as well as in our gut, it becomes highly necessary to have proper techniques to detect, isolate and identify Viruses or VLPs from the river water sample so that using them we can take a step towards making Ganga pathogen-free. This will help in making the use of Ganga water for various purposes safer. Various methods are already in use which detects viral samples from water samples. Some of which are PCR (RT PCR, qPCR), flow cytometry, MPN studies, plaque assays, observation of cytopathogenic effects, metagenome-based pathogen surveillance etc. The already in use methods need to be practiced more efficiently and many more methods need to be introduced for studying the vast array of virus-mediated Ganges purification.

CONCLUSION

It has been established and widely accepted that Ganga has self-purificatory activities owing to the presence of certain viral strains into the water. The high abundance of the virome in the Ganges as compared to other rivers sheds light on this belief. Certain viruses are capable of digesting pollutants and contaminants including heavy metals and dangerous pathogens. Due to the presence of these kinds of viruses along with deadly pathogens and high order pollutants in the Ganges, the use of the river water is not life-threatening. Although much more shreds of evidence are required for the proper implementation of virome-mediated purification projects on the river. It is necessary to identify those viral species which are directly or indirectly involved in cleansing actions of the Ganges and use them for cleaning the river, making it pathogen-free and thus safer for domestic, agricultural as well as industrial use.

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Conflict of Interest

Author declare that they have no conflict of interest.

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