RHIZOSPHERE MICROBIOME: AN EMERGING FRONTIER IN CAUSING AND CURING INFECTIOUS DISEASES

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Received: 15 February 2018, Revised and Accepted: 16 March 2018

ABSTRACT

Prevalence of pathogenic microorganisms in the rhizosphere causing infectious diseases in plants and humans has increased considerably due to a high content of nutrients. Such pathogenic infections are of huge concern in agriculture, health care, and medical arenas. Rhizosphere microbiome is a “microbial hotspot,” not only for pathogenic microorganism but also for unlimited beneficial microorganisms. Therefore, this microbiome has immense potential in the shaping of earth from natural vegetation to the intense agricultural production to human health. Rhizosphere microorganism from unexplored habitats is a promising approach to overcome the escalating threat of such pathogenic infections. Hence, efforts are being made to isolate more and more rhizobacteria that are beneficial for better plant productivity and for treating human diseases. Thus, present review highlights and discusses the available literature on beneficial/pathogenic microorganisms belonging to rhizosphere and their impact on plants and human diseases. Furthermore, it sheds light on how this novel knowledge helps in deriving maximum benefits out of this naturally occurring population for the betterment of plant and human health.

Keywords: Beneficial microbes, Health, Pathogenic, Rhizosphere, Rhizobacteria.

INTRODUCTION

Recent reviews of the scientific literature have highlighted that the proliferation of rhizospheric pathogenic microorganisms affecting both plants and humans (particularly in immune compromised individuals) has increased significantly during the past few decades [1-3]. Infections by these microorganisms are of grave concern when it comes to areas such as agriculture, medicine, and health care. The number of therapeutic options for the treatment of these infections is quite limited. In fact, presently available drugs are not optimal due to their low efficacy, toxicity and the emergence of drug resistance in pathogenic microbes [4]. Hence, it has become imperative to look for novel antimicrobials from the unexplored habitats that can help in the future to mitigate the increasing threat of drug-resistant strains related to human and plant pathogens.

The considerable amount of research is going on worldwide in search of antimicrobial agents which could counter the threat of infectious diseases. Soils have been continuously screened in the past for potent microorganisms, and nowadays major focus has shifted to rhizosphere as it represents one of the richest habitats of microbes. Recent metagenomics and meta-transcriptomics approaches have also been explored on more rhizosphere microbiota [4-6] as shown in (Table 1). Bacteria, algae, fungi, and protozoa are some of the microorganisms which are associated with colonization in plant roots. These microorganisms have beneficial, harmful, and/or neutral effects on the plant growth and development [7,8] as shown in Fig. 1. Applications of these microbial populations enhance plant growth and provide defense against pathogenic microorganisms, facilitating the nutrient acquisition and thus help plants withstand stressful conditions [9-12]. Another type of microorganisms present in the rhizosphere is phytopathogens and opportunistic pathogens which have a severe impact on plant and human health. Therefore, understanding the basic mechanism and characteristics of rhizosphere microbiome is a major task to maintain the plant productivity and to defend human wellbeing. The present review highlights and discusses the present knowledge of beneficial and pathogenic rhizospheric microorganisms and their impact on human and plant diseases. Moreover, we have tried to shed light on how this knowledge could be helpful in deriving maximum benefits out of this naturally occurring population.

IMPACT OF RHIZOSPHERE MICROBIOME ON PLANTS

The synthesis and efficiency of the natural plant communities (i.e., biomass) are directly and/or indirectly influenced by rhizosphere microbiome [28]. Pathogens (human as well as a plant) also form part of the plant associated microbiomes besides the majority of beneficial and neutral inhabitants. These pathogenic microbes are the subject of huge concern, particularly for plant growth and the environment [3]. Examining these microorganisms by unraveling their likely association with plants opened new doors for fascinating study related to rhizosphere research. Therefore, here, we will discuss the role of pathogenic microbes in the rhizosphere and how beneficial microbes from same or different plant rhizosphere can be useful in managing these problems.

Pathogenic interactions

One of the major obstacles to the production of adequate supplies of food, feed, fiber, and fuel is the damages caused by phytopathogens. Most studies till date on plant pathogen revealed that rhizosphere can be considered as the infectious courtyard where soil-borne pathogens, including bacteria, fungi, oomycetes, and nematodes entrenched a parasitic association with the plant. Pathogens emit particular classes of effectors into the apoplast or inside the plant cell to incite infections in the plant associated microbiomes besides the majority of beneficial and neutral inhabitants. These pathogenic microbes are the subject of huge concern, particularly for plant growth and the environment [3]. Examining these microorganisms by unraveling their likely association with plants opened new doors for fascinating study related to rhizosphere research. Therefore, here, we will discuss the role of pathogenic microbes in the rhizosphere and how beneficial microbes from same or different plant rhizosphere can be useful in managing these problems.

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The considerable amount of research is going on worldwide in search of antimicrobial agents which could counter the threat of infectious diseases. Soils have been continuously screened in the past for potent microorganisms, and nowadays major focus has shifted to rhizosphere as it represents one of the richest habitats of microbes. Recent metagenomics and meta-transcriptomics approaches have also been explored on more rhizosphere microbiota [4-6] as shown in (Table 1). Bacteria, algae, fungi, and protozoa are some of the microorganisms which are associated with colonization in plant roots. These microorganisms have beneficial, harmful, and/or neutral effects on the plant growth and development [7,8] as shown in Fig. 1. Applications of these microbial populations enhance plant growth and provide defense against pathogenic microorganisms, facilitating the nutrient acquisition and thus help plants withstand stressful conditions [9-12]. Another type of microorganisms present in the rhizosphere is phytopathogens and opportunistic pathogens which have a severe impact on plant and human health. Therefore, understanding the basic mechanism and characteristics of rhizosphere microbiome is a major task to maintain the plant productivity and to defend human wellbeing. The present review highlights and discusses the present knowledge of beneficial and pathogenic rhizospheric microorganisms and their impact on human and plant diseases. Moreover, we have tried to shed light on how this knowledge could be helpful in deriving maximum benefits out of this naturally occurring population.

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**Pathogenic interactions**

One of the major obstacles to the production of adequate supplies of food, feed, fiber, and fuel is the damages caused by phytopathogens. Most studies till date on plant pathogen revealed that rhizosphere can be considered as the infectious courtyard where soil-borne pathogens, including bacteria, fungi, oomycetes, and nematodes entrenched a parasitic association with the plant. Pathogens emit particular classes of effectors into the apoplast or inside the plant cell to incite infections in the root tissue [29,30]. From, the past two decades the effect of pathogenic fungi on plant health has expanded significantly. There are two major groups of plant pathogens, i.e., fungi and nematodes [31]. The fungal and oomycetes pathogens, i.e., Aspergillus, Fusarium, Phytophthora, Colletotrichum, Pythium, Verticillium, Rhizopus, and Rhizoctonia present in rhizosphere crops, and few bacterial genera (i.e., Pectobacterium carotovorum, Dickeya dadantii,Ralstonia solanacearum, Pectobacterium atrosepticum, and Dickeya solani) are responsible for significant loss of grain worldwide and result in economic repercussions [31].
Methodology

16S rRNA gene pyrosequencing

Twenty-six phyla were identified from 5089 16S rRNA gene pyrosequencing reads, and 1917 taxa were identified by identification of 33346 bacterial and archaeal OTUs with the highest number of unclassified groups (9%). Betaproteobacteria were identified as most dynamic taxa in disease suppression.

Detection of 2432 OTUs with the highest number of taxa as detected in soil. Bacteroidetes, and Proteobacteria were dominant and accounted for 77.1% of the bacterial community. Detection of 33346 bacterial and archaeal OTUs with the dominance of Proteobacteria (46%), Actinobacteria (3%), Micromonosporaceae, Streptomyces, and Pseudomonadaceae bacterial families was found to exhibit the strongest response at the potato cultivar level.

Detection of 1000 OTUs was identified in the root compartment with the dominance of Betaproteobacteria and Acidobacteria. Acidobacteria, Actinobacteria, and Proteobacteria were found to be most abundant bacterial groups. Identification of 18783 bacterial OTUs with the highest number of expected rhizosphere-competent phyla (phylum Proteobacteria 38%), and least to Acidobacteria (3%). Micromonosporaceae, Streptomyces, and Pseudomonadaceae bacterial families was found to exhibit the strongest response at the potato cultivar level.

Identification of 1917 taxa by 16S rRNA gene pyrosequencing

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Table 1: Bacterial and archaeal taxa recognized in the rhizosphere

| Host                        | Methodology                  | Rhizosphere microbiome composition                                                                 | References |
|-----------------------------|------------------------------|-----------------------------------------------------------------------------------------------------|------------|
| Oat microcosms             | 16S rRNA gene microarray     | Identification of 1917 taxa by Firmicutes and Proteobacteria community dominance. Detection of less expected rhizosphere-competent phyla (Actinobacteria, Verrucomicrobia, and Nitrospirae). | [13]       |
| D. antarctica and C. quitensis | 16S rRNA gene pyrosequencing | Firmicutes and seldom detected groups Acidobacteria (phylum Proteobacteria), Faecalibacterium (phylum Firmicutes), and Bifidobacterium (phylum Actinobacteria) were found to be most predominant genera. | [14]       |
| Oak (forest soil)          | 16S rRNA gene pyrosequencing | Predicted predominant phyla were found to be Actinobacteria (11%), Acidobacteria (24%), Proteobacteria (38%), and including a high proportion of unclassified bacteria (20%). Identification of 5619 OTUs in one of the bacterial community. | [15]       |
| Sugar beet agriculture soil | 16S rRNA gene microarray     | Detection of 33346 bacterial and archaeal OTUs with dominance of Firmicutes (20%), Proteobacteria (39%), Actinobacteria (9%), and Betaproteobacteria were identified as most dynamic taxa in disease suppression. | [16]       |
| Potato field soil          | 16S rRNA gene microarray     | Detection of 2432 OTUs with the highest number of taxa as detected in soil. Bacteroidetes, and Proteobacteria were dominant and accounted for 77.1% of the bacterial community. Detection of 33346 bacterial and archaeal OTUs with the dominance of Proteobacteria (46%), Actinobacteria (3%), Micromonosporaceae, Streptomyces, and Pseudomonadaceae bacterial families was found to exhibit the strongest response at the potato cultivar level. | [17]       |
| R. mangle and L. racemosa (mangrove) | Archaeal 16S rRNA gene pyrosequencing | Identification of 300 archaeal OTUs along-with detection of Halobacteria, Methanobacteria, Methanomicrobia, and Thermoprotei classes. | [18]       |
| Potato (field soil)        | Pyrosequencing                | Identification of 55121 OTUs with Actinobacteria and Alphaproteobacteria as most abundant groups. | [19]       |
| R. mangle (mangrove)       | 16S rRNA gene pyrosequencing | Most abundant phylum detected was Proteobacteria. | [20]       |
| M. carnea (cactus) (semi-arid environment) | 16S rRNA gene pyrosequencing | Most abundant phylum detected was Proteobacteria. | [21]       |
| A. thaliana (cologne and gohm soils) | 16S rRNA gene pyrosequencing | Estimation of 1000 OTUs was identified in the root and rhizosphere compartments with the dominance of Acidobacteria, Proteobacteria, Planctomycetes, and Actinobacteria. Most prevailing phyla includes Proteobacteria, Actinobacteria, and Bacteroidetes. Identification of 18783 bacterial OTUs with the dominance of Bacteroidetes, Actinobacteria, and Proteobacteria. | [22]       |
| A. thaliana (Mason farm and clayton soil) | 16S rRNA gene pyrosequencing | Identification of 479 OTUs belonged to seven phyla with the dominance of Proteobacteria, Firmicutes, and Actinobacteria. | [23]       |
| S. tuberosum in high andes | 16S rRNA gene pyrosequencing | Identification of 479 OTUs belonged to seven phyla with the dominance of Proteobacteria, Firmicutes, and Actinobacteria. | [24]       |
| S. saponaria L.            | 16S rRNA gene pyrosequencing | Twenty-six phyla were identified from 5089 sequences of 16S rRNA gene. Most predominance was Actinobacteria (33.54%), Acidobacteria (22.62%), and Proteobacteria (24.72%). | [25]       |
| L. japonicas               | 16S rRNA genes               | Two nodule-enriched OTUs among a total of 1834 OTUs. Mesorhizobium members representing the most abundant taxa. Three phyla Proteobacteria, Cyanobacteria, and Bacteroidetes were dominant and accounted for 77.1% of the bacterial community. Detection of 33346 bacterial and archaeal OTUs with the dominance of Proteobacteria, Bacteroidetes, and Actinobacteria accounted for 55.1% of taxa as detected in soil. | [26]       |
| S. oleracea L., cv. Racoon | 16S rRNA genes               | Two nodule-enriched OTUs among a total of 1834 OTUs. Mesorhizobium members representing the most abundant taxa. Three phyla Proteobacteria, Cyanobacteria, and Bacteroidetes were dominant and accounted for 77.1% of the bacterial community. Detection of 33346 bacterial and archaeal OTUs with the dominance of Proteobacteria, Bacteroidetes, and Actinobacteria accounted for 55.1% of taxa as detected in soil. | [27]       |

Beneficial effect of rhizosphere microbial community on plant

Plant rhizosphere not only comes across as one of the natural reservoirs for disease-causing microorganisms but also they are also the habitat for an unlimited beneficial microorganisms with the larger biotechnological applications to enhance plant growth and productivity. However, the main challenge in promoting their possibilities lies in understanding the impact of these communities on plant health and productivity.

D. antarctica: Deschampsia antarctica, C. quitensis: Colobanthus quitensis, R. mangle: Rhizophora mangle, L. racemosa: Laguncularia racemosa, M. carnea: Mammillaria carnea, A. thaliana: Arabidopsis thaliana, S. tuberosum: Solanum tuberosum, S. saponaria L., S. oleracea L., L. japonicas: Lotus japonicas, S. oleracea L., Spinacia oleracea L., OTUs: Operational taxonomic units.
Rhizosphere microorganisms have been widely considered for their beneficial effects on plant development and wellbeing and are observed to be required in biofertilization, incitement of root development, rhizoremediation, control of abiotic/biotic stresses, and diseases. These mechanisms have been recognized to be carried out by rhizobacteria belonging to Proteobacteria and Firmicutes (Pseudomonas and Bacillus), fungi from Deuteromycetes class (Gliocladium and Trichoderma), and Sebacinales order (Periformospora) [32].

Rhizosphere microbiome can significantly affect plant productivity by controlling the nutrient status of the plants. Nitrogen fixing bacteria such as Mycorrhiza and Rhizobium, present in the rhizosphere of various crop plants help in the uptake of phosphorus and nitrogen, respectively [33-35]. *Rhizobium* and *Bradyrhizobium* found in the root nodules of leguminous plants converts atmospheric nitrogen into useful key compounds that can be utilized by the plants and humans [36]. Inoculation of plant growth promoting rhizobacteria (PGPR), i.e., *Bacillus pumilus* 51R1 has been reported to be an alternative method for naturally fixing atmospheric nitrogen in delaying the nitrogen remobilization in mature plants to get a higher yield with less utilization of nitrogen fertilizers [37]. Some other PGPR were also found to release organic phosphate or solubilize the insoluble phosphate, thereby enabling the plant growth and productivity [38]. *Pseudomonas, Penicillium, Bacillus, Micrococcus, Sclerotium, Flavobacterium, Aspergillus,* and *Pusarum* have been testified to be highly involved in the solubilization process [39,40]. Various Siderophores producing rhizobacteria such as *Bacillus subtilis* (strain GB03), and *Paenibacillus polymyxa* (BFC01) have been found to activate iron acquisition machinery to increase metal ion assimilation in *Arabidopsis*. A study conducted on inoculation of shoot propagated cassava with *B. subtilis* (strain GB03) has exhibited higher iron accumulation following 140 days of plant development as detected by X-beam microanalysis and total foliar iron analysis. Whereas BFC01-inoculated plants demonstrated that BFC01 transcriptionally actuates the Fe-insufficiency instigated translation Factor 1, in this manner up directing the outflow of IRT1 and PRO2. Thusly, BFC01-inoculated plants have more endogenous Fe and expanded photosynthetic limit under basic conditions when contrasted with control plants. It ultimately results in growth promotion and increased photosynthetic efficiency in *Arabidopsis* plants [41,42]. It has also been elucidated that the inoculation of arbuscular mycorrhizal fungi with plant enhances plant growth under high salt concentration [43]. A study conducted by a team of a biologist, using rhizosphere technology elucidates that *Pseudomonas aeruginosa, Pseudomonas fluorescens, Mycobacterium spp., Haemophilus spp., Rhodococcus spp., and Paenibacillus spp.* are some of the most commonly studied polyaromatic hydrocarbons degrading bacteria in the rhizosphere [44].

Apart from the above mentioned beneficial effects of rhizosphere microbiome they are also seem to be frontline defense toward phytopathogens. One of the most widely recognized biocontrol mechanisms driven by PGPR includes antibiotics, (inhibition of the pathogenic microbial growth by producing antibiotics), biosurfactants, and volatile organic compounds. Production of metabolites, i.e., antibiotics by rhizospheric bacteria, is often implicated as an important bio-control mechanism because it is relatively simplest and most effective mechanism to study. A work carried out by Sahoo et al., on PGPR (*Bacillus amyloliquefaciens* 937b and *B. pumilus* SE-34) showed protection against tomato motte virus (TMV) [45]. Another study carried out on *Streptomyces cacaoi strain M-20* isolated from *Avicennia marina* rhizosphere has also shown antifungal activity against phytopathogen *Fusarium oxysporum*, which was reported to be responsible for the significant reduction in legume production [46]. Some studies had observed that the mycorrhizae bacteria provide resistance against fungal pathogens by inhibiting the growth of many root pathogens such as *Rhizoctonia solani, Pythium spp., F. oxysporum,* and *Heterobasidion annosum.*

**Fig. 1: Graphical representation of the functions and outcome of rhizosphere microorganisms**

**Impact of rhizosphere microbiome on human health**

Rhizosphere microbiomes serve not only as sources of plant pathogens and beneficial microbes but they have also been found to function as a foundation as well as treatment of opportunistic human pathogens as discussed here.

**Rhizosphere, a reservoir of opportunistic human pathogens**

Opportunistic human pathogens normally does not harm its host, but can cause diseases in the individuals with weakened immune system, particularly those undergoing blood and bone marrow transplantation, major surgery (especially gastrointestinal surgery); patients with AIDS, solid-organ transplantation, neoplastic disease, premature infants, and patients receiving immunosuppressive therapy [47,48]. Infections by these pathogens lead to serious or even deadly complications in patients with compromised immune systems. In the past two decades, the effect of opportunistic infection on human wellbeing has expanded significantly. In spite of this fact, little is known about the nature and the pathogenesis of these emergent pathogens. Some of these opportunists originate in the rhizosphere, which is the zone around plant roots [1,49]. A number of studies on rhizosphere microbiome highlighted the prevalence of opportunistic human pathogens in wild and cultivated plant species (such as *P aeruginosa, Burkholderia cepacia,* or *Stenotrophomonas maltophilia* [49]. However, there is relatively less information available regarding the virulence, adaptation, and survival of other bacterial species that were identified in rhizosphere and have been...
associated with skin, urinary tract infections, and wound (e.g., *Proteus vulgaris* and *Bacillus cereus*) [49,50]. Several factors responsible for the incidence of opportunistic human pathogens in the rhizosphere include higher nutrient content, access to water for dispersal and prevention from dehydration, protection from ultraviolet radiation [49,51]. A study carried out by a scientist suggested that the roots release a chemical stimulator that activates chemotaxis in *S. enterica* which in turn switches on the genes responsible for adherence to plant surfaces. Numerous other genes and characters have also been identified to be responsible for the attachment of the opportunistic pathogens to plant surfaces, together with adhesins, capsule production and fimbiae [52]. Polyphasic approaches, conducted on genotype PaBP35, comprising rDNA sequence analysis, BOX-polymerase chain reaction, comparative genome hybridization analysis and multilocus sequence typing, discovered the uniqueness of *P. aeruginosa* strains on behalf of the clinical habitats. However, further analysis revealed that certain traits of PaBP35, such as growth at 25–41°C, resistance to antibiotics, and production of phenazines, and rhamnolipids besides exhibiting cytotoxicity on mammalian A549 cells, were similar to other *P. aeruginosa* strains [53]. Recently, more studies on polyphasic approaches on rhizosphere microbiome revealed that *Rhizobium pusense* is the main human pathogen within *Agrobacterium* (*Rhizobium*) spp. [54]. Some other phytopathogenic fungus, such as *Pseudomonas solani* and *Colletotrichum*, are also considered as human pathogens. Recent studies have also highlighted as to how bacteria (*Vibrio parahaemolyticus*) developed a mechanism to quench iron from the human host using siderophores and xenosiderophores, prototases, and iron-protein receptors [55]. Siderophore (yersiniabactin) delivered by uropathogenic *Escherichia coli* bind with copper particles during human diseases. Thus, protect *E. coli* from copper lethality and redox-based phagocytosis which makes it distinct from other *E. coli* siderophores [56].

**Role of rhizosphere microbiome in fighting opportunistic infections**

Plant-associated microbiome leads to significant outbreaks of contagious diseases in transferring transfer of potential pathogens [54], they also act as a source of beneficial bacteria that inhibits human pathogens and therefore can positively influence human health [57]. Studies on *Burkholderia* genus (naturally present in the rhizosphere of crop plants) revealed that *Burkholderia contaminans* (MS14) strain produces an antifungal compound, occidofungin, which triggers considerable antifungal activities against a wide range of invasive fungal pathogens (plant and animal) [58]. Similar studies were carried out on carried on sagebrush rhizospheric soil isolates (phenol-resistant and humic acid, vitamin) had revealed the broad-spectrum antifungal, antibiotic activity against *Pythium ultimum* and *Candida albicans* strains. Phylogenetic analysis of these isolates showed a close resemblance to *Streptomyces violaceogensifer* clade [59]. The metabolites of *Streptomyces cellulosae* VJDS-1 isolated from mangrove soil of *Nizampatnam*, Guntur, (Andhra Pradesh), India, had also reported the antimicrobial against Gram-positive (*Staphylococcus aureus* and *Bacillus megaterium*), Gram-negative bacteria (*Xanthomonas campestris* and *P. aeruginosa*, *E. coli*), and fungi (*Aspergillus niger*, *C. albicans*, *P. solani*, and *P. oxybsporum*) [60]. Antibiotics, including amphotin, 2,4-diacylphloroglucinol, pyrroloeterin, pyrrolinrin, tensin, tropolone, kanosamine, Oligomycin A, xanthobacin, and *Zwittermicon A* identified in antagonistic Gram-negative bacteria, such as *Pseudomonads, Bacillus, Streptomyces*, and *Stenotrophomonas*, are multidrug-resistant against human pathogenic bacteria [61]. Biosurfactants, produced mostly by rhizobacterial population, were also found to have antimicrobial activity against human pathogenic Gram-positive (*S. aureus*) and Gram-negative (*P. vulgaris*) bacteria [62]. Recently, targeting iron acquisition in the cystic fibrosis lung has been found to be a novel therapeutic strategy for cystic fibrosis and aspergillosis [63]. Hence, an antibiotic produced by rhizosphere microbiome is a “hotspot” for potential therapeutic developments, yet, in-depth knowledge is required on these antibiotics.

**CONCLUSION**

The significance of the rhizosphere microbiome in the functioning of plant biological communities has been broadly recognized. Traditional ways to deal with disentangle these functions are constrained in their ability and for most of rhizosphere microorganisms, no information exists. There are still certain aspects which need further investigations to derive maximum benefits such as improved plant growth and human health out of these naturally occurring populations, particularly under distress and unfavorable ecological conditions. The majority of the work on this topic has focused on the functional roles of the single microbial population with plants, mostly because of the methodological restriction associated with nonculturable microbial populations. A combination of traditional and next-generation sequencing techniques to identify and characterize the organism/community ecology and physiology will help in understanding the microbial life and their role in the rhizosphere, thereby, opening new opportunities for novel discoveries. Hence, we conclude that comprehensive knowledge of rhizosphere microbiome can be useful in many areas including the discovery of novel drugs, inhibiting the proliferation of human pathogens in plant environments and protection from current and future emerging diseases.

**ACKNOWLEDGMENT**

The authors would like to thank M.D. University, Rohtak, India, for providing University Research scholarship.

**CONFLICTS OF INTEREST**

The authors confirm that this article content has no conflicts of interest (none to declare).

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