

Harnessing Plant Plasmid Curing Activity as an Alternative Approach to the Antibiotic Resistance Problem

Opinion

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Opinion

Control of bacterial pathogens has become increasingly difficult, as many pathogens have acquired multiple antibiotic resistance and virulence traits, largely by plasmid mediated gene transfer systems [1]. Such plasmid mediated mechanisms can lead to transfer of multiple antibiotic resistance and virulence traits to related pathogens. Plasmid curing (reduction or elimination) activity has been demonstrated in four different plant species, presumably as a defense against bacterial and viral diseases.

Could the increasing problem of plasmid mediated antibiotic resistance in humans and animals be addressed by employing plant defense systems? This approach would be directed to curing the bacteria of the plasmids that carry traits for antibiotic resistance and hypervirulence, rather than to directly attack their bacterial carriers. Researchers have reported that root extracts of *Aplinia galangal* were capable of curing plasmids in a variety of multidrug resistant, clinically relevant bacteria [2]. Similar plasmid curing characteristics have also been discovered in two other plants, *Discourdea* and *Plumbago* [3]. Experiments with extracts of Chitrak from these plants showed that *Salmonella typhi* (strain R136) was cured of virulence plasmids [4]. Fermented olive leaves have been shown to have potential antibacterial activities in plasmid profiling and plasmid curing in *Staphylococcus* and *Streptococcus* mutants [5]. Xiao et al, [6] reported plasmid curing activity in Chinese ginger.

Our interest has been focused on a search for plasmid curing systems existing in cultivars of crop plants, especially those being used in feed and food systems. We initially observed that a certain heirloom cultivar accession of Ethiopian barley demonstrated effective bacterial plasmid curing in leaf extracts [7]. Ethiopia was one of the two geographic regions where 8,000 years of domestication of barley took

place [8]. We considered the possibility that as barley populations were domesticated and served as a main food source, they may have also served as a source of plasmid curing activities. During the gradual domestication of barley, populations may have been repeatedly selected for resistance to several common bacterial pathogens that harbored plasmids. In this way, some land race populations of barley could have contributed to maintaining the health of the subsistence farming communities. Selections from these land races of barley could now serve as a beneficial staple food for humans and as a feed for domesticated animals now and in the future.

We have determined that a leaf extract of a certain barley cultivar (MSU 121) elicit curing of *E. coli* plasmids carrying both ampicillin resistance traits and green fluorescent protein plasmid markers (Figure 1). The initial results showed a modest but positive effect. We have determined in feeding studies that a leaf extract of the same cultivar of barley has been extremely effective in curing calf and lamb scours (manuscript in preparation).

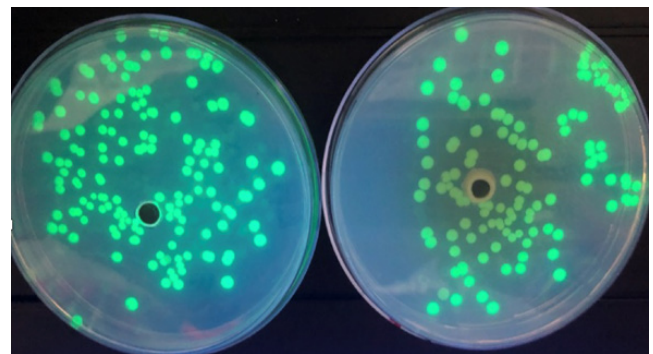


Figure 1: Green Fluorescent Protein carried on a plasmid in control and *E. coli* bacteria colonies treated with leaf extract of barley MSU-121. The colony count of MSU-121 treated cells is observed to be lower 24 hours after the barley extract has been placed onto the dish.

We wish to alert other researchers that they can use similar assays to screen candidate plant-based feed components for plasmid curing activities. There are several different molecular mechanisms that elicit plasmid curing in microbes and these can be deployed in combination. Potentially, these are causally attributed to several viruses and several types of bacteria. This plant-based approach to “kill the messenger not the bacterium” may be a strategy to consider for those researchers that are confronting the dilemma of ever-increasing antibiotic resistance. This simple yet ingenious biological approach could potentially change the approach of attacking and eradicating antibiotic resistance.

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