Role of food chain containing lactic acid bacteria in antibiotic resistance

The emergence of antibiotic resistance among microorganisms has been part of various recent scientific deliberations. Consequences of antibiotic resistance include increased morbidity and mortality, enhanced stay in hospitals leading to increased duration and cost of treatments. Irrational use coupled with lack of development of new antibiotics has made the situation worrisome. While clinical organisms have been considered primary culprits contributing to emergence and transfer of resistance, the role of food chain containing commensal organisms such as lactic acid bacteria has not received due attention.

Lactic acid bacteria which include *Lactobacillus*, *Enterococcus*, *Pediococcus* and *Bifidobacteria* are a significant part of the food chain and widespread in human, animal and plant microflora. These aerotolerant anaerobic ubiquitous organisms have the ability to convert carbohydrates into lactic acid and by virtue of such metabolism have been used for centuries as part of fermented foods as starter cultures. Recently their commercial applications as probiotics (foods containing live organisms to derive health benefits by positively modulating gut microflora) has increased manifold. The US probiotic market is expected to be worth US$ 4.6 billion by 2010 (ref. 2). Indian market is also witnessing a surge of probiotic products with Amul, Nestle and Yakult launching new products. These organisms enjoy time tested reputation of being safe thus given GRAS (Generally Recognized As Safe) status by US FDA. But their role vis-à-vis own antibiotic resistance and transfer of resistance via food chain is yet to be ascertained.

Lactobacilli have been found to be resistant to vancomycin, bacitracin, metronidazole, norfloxacin, streptomycin and clindamycin. Similarly bifidobacteria have shown resistance to vancomycin, tetracycline, fusidic acid, kanamycin, gentamycin, metronidazole, norfloxacin, streptomycin, nalidixic acid and polymyxin B. Resistance to antibiotics in lactobacilli is attributed to common mechanisms such as decreased uptake and increased export of antibiotics, inactivation or modification of target site, modification of antibiotic, prevention of activation of antibiotic. Besides, there are few known specific mechanisms such as vancomycin resistance which is due to presence of D-Ala-D-lactate in peptidoglycan in place of D-Ala-D-Ala dipeptide. Also, lactobacilli are usually considered resistant to most inhibitors of nucleic acid synthesis and this resistance is considered intrinsic. Thus there are some key questions to be answered such as intergenus and intragenus variability in resistance and lack of complete understanding of mechanisms underlying resistance. The vancomycin resistance in lactic acid bacteria is of significant concern as this is the only antibiotic used to treat multiple drug resistant *Staphylococcus aureus*. Also, in *Lactobacillus*, *Pediococcus* and *Leuconostoc*, the resistance is intrinsic but in *Enterococcus* it is coded by a transferable plasmid.

Lactic acid bacteria are also potential candidates for horizontal transfer of antibiotic resistance as they are consumed live along with food and reside in close proximity to diverse organisms in various ecological niches. Also, the genetic elements like self-transmissible plasmids, conjugative transposons, involved in horizontal gene transfer are present in lactic acid bacteria. The presence of acquired antibiotic resistance genes in *Lactococcus lactis* plasmid pK 214 showing high homology to pathogenic organisms *S. aureus* and *Listeria monocytogenes* indicates movement of genes across various genera involved in food chain. Lactobacilli have been shown to possess different acquired resistance genes namely tet(M), tet(S) for tetracycline, erm(B) for erythromycin. Some studies have indicated *in vitro* horizontal transfer of resistance from lactic acid bacteria.

Overall, lactic acid bacteria have a significant role to play in maintaining health but there is evidence to suspect their role in transfer of antibiotic resistance. The situation is compounded by various constraints such as lack of breakpoints and standards, lack of uniform evaluation procedures and incomplete understanding of intrinsic and transferable resistance. International initiatives like Assessment and Critical Evaluation of Antibiotic Resistance Transferability in Food Chain (ACE-ART) have been taken up to address the issue but there is requirement at the national level too to anticipate contribution of food chain and its components in overall proliferation of antibiotic resistance and strict regulations governing use of such organisms via food chain is required.


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CURRENT SCIENCE, VOL. 97, NO. 12, 25 DECEMBER 2009 1703