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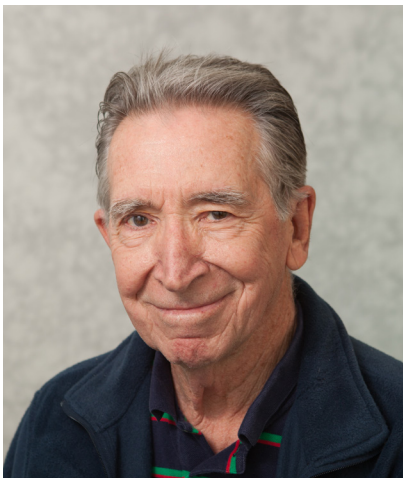

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A novel class of antibacterial substances has been discovered in a collaborative project between the Chemistry and Biology Departments at Grand Valley State University (GVSU). These compounds do not rely on currently accepted antibiotic chemical structure but seemingly have a mechanism of action different from understood mechanistic pathways for treatment of infections and are readily synthesized, avoiding complex, stereoselective, multi-step synthesis.

This new class of antibiotics is composed of chemical derivatives of the telomerase inhibitor BIBR1532 [US Patent 6362210]. Our compounds demonstrated *significant antimicrobial activity* against a group of Gram-Positive microorganisms. The antibiotic's minimum inhibitory concentrations (MICs) against these bacteria are equivalent to existing antibiotics (2-78 ug/ml). In subsequent *in-vitro* tests these compounds showed activity against methicillin-resistant *Staphylococcus aureus* (MRSA), vancomycin resistant enterococci (VRE), *Bacillus anthracis* (anthrax), and *Clostridium difficile* (Cdiff). The antibacterial activity against MRSA, VRE, and Cdiff strains of bacteria is promising as it demonstrates the ability of BIBR 1532 to inhibit microbial growth in organisms with resistance to common antibiotics.

In 2008, GVSU patented this antibiotic family. Since then, we determined that the frequency of bacterial resistance to this class of antibiotics is extremely low. Over 70 compounds were tested for antibacterial activity. Sixty demonstrated antibacterial activity and of these 18 were more thoroughly tested against 25 bacterial and fungal strains. We discovered that a number of compounds had low minimum inhibitory concentrations (MICs) against *Staphylococcus aureus* (including MRSA strains), *Bacillus anthracis* (anthrax), *Clostridium difficile*, and *Streptococcus pneumonia*. These results were encouraging as they demonstrate multiple bacterial targets with low drug concentrations (2-8 ug/ml).

Additionally, we tested six compounds in acute *in vitro* toxicity screening in a rat hepatoma (H4IIE) cell line at 24 hour exposure. All compounds demonstrated minimal toxicity to the cell line. These toxicity results demonstrate that potential negative side-effects to patients appear to be minimal.

Further testing of our antibiotics revealed significant binding to human serum protein. This is potentially problematic in clinical use as there is less available compound in the blood. There are conflicting opinions as to the significance of binding to serum protein. For example, nine of the top 10 best-selling small molecule, single agent prescription drugs of 2006 had 90% or greater binding to serum protein and seven of the top ten had 95% or greater [Rydzewski, R.M., 2008]. A potential problem exists and we continue to work towards lowering this binding to increase potential available drug concentrations in the blood.

*This scholar and faculty mentor have requested that only an abstract be published.