Currently approved drugs found effective in laboratory mice against bioterror threats

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In the most extensive screen of its kind, Texas Biomed scientists in San Antonio have demonstrated the feasibility of repurposing already-approved drugs for use against highly pathogenic bacteria and viruses. The pathogens included emerging diseases and potential bioterror threats ranging from anthrax to the Marburg and Ebola viruses.

In testing a library of 1,012 Food and Drug Administration-approved drugs, commonly used for treatment of every-day ailments like diabetes and high blood pressure, the scientists found that ten were active against two or more bacteria and that 24 were active against two or more viruses.

Two drugs were found to be the most potent compounds in protecting mice against anthrax while one drug, chloroquine, once used to treat malaria, protected mice against Ebola virus, said Robert Davey, Ph.D., a Texas Biomed virologist.

The new study, which included authors Jean Patterson, Ph.D., and Ricardo Carrion, Ph.D., both of Texas Biomed, appears in the April 2013 issue of the journal *PLOS ONE*. Their findings came from a collaborative effort among Texas Biomed, independent research institute SRI International and the U.S. Army Medical Research Institute of Infectious Diseases. It was supported by funds from the Defense Threat Reduction Agency, the Defense Department's agency for countering weapons of mass destruction.

"Repurposing of existing drugs that may have unanticipated activities as potential countermeasures is one way to meet this important goal, since currently approved drugs already have well-established safety and pharmacokinetic profiles in patients, and manufacturing and distribution networks," the authors wrote. "Therefore, approved drugs could rapidly be made available for a new indication in an emergency."

The scientists found a variety of hits against two or more of these bio-threat pathogens, which were validated in secondary tests. As expected, antibiotic compounds were highly active against bacterial agents, but the researchers did not identify any non-antibiotic compounds with broad spectrum antibacterial activity.

Lomefloxacin and erythromycin were found to be the most potent compounds in protecting mice against anthrax. Lomeflaxacin is used to treat bronchitis and urinary tract infections. Erythromycin is used against respiratory tract infections.

The most noteworthy antiviral compound identified was chloroquine which disrupted virus entry and replication in cells of two or more viruses in vitro and protected mice against Ebolavirus.

Due to the demanding complexity of working with these agents under laboratory conditions as well as the fact that human drug clinical trials cannot be ethically conducted for any of these agents, conventional drug discovery and development approaches are particularly challenging. For these agents, the FDA must evaluate the efficacy of drugs on the basis of their activities in appropriate animal models, under agency guidance. Thus, drug-repurposing offers many advantages, particularly given the fact that human safety studies have already been conducted.

Members of the Texas Biomed team are presently pursuing whether the other drugs could be equally useful for treatment of these viruses.

"It would be important to determine if a combination of drugs could be more potent than each individual drug," Davey said. "Such synergy, when seen, usually means you can lower the dose of each drug and still have a big impact on the disease while minimizing bad side effects. Such work could prove useful as an easy frontline defense against these viruses."

More information: www.plosone.org/article/info%3Adoi%2F10.1371%2Fjournal.pone.0060579

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