New drug leads could battle brain-eating amoebae

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Brain-eating amoebae can cause particularly harmful forms of encephalitis, and more than 95% of people who develop these rare but devastating infections die. Despite the high mortality rate, there is

currently no single effective drug available to fight these microbes. Now, however, researchers have designed some new compounds that show promise in the laboratory as treatments, according to a report in *ACS Chemical Neuroscience*.

Naegleria fowleri and *Balamuthia mandrillaris* are two types of amoebae that can cause primary amoebic meningoencephalitis and granulomatous amoebic encephalitis. They are single-celled microorganisms that live in water and soil, and can enter the body through the nose or open wounds. These pathogens can then move to the central nervous system, where they destroy brain cells. In the very few cases that have been treated successfully, patients were given high doses of many different antimicrobials. However, these drugs generally lack specificity and can have toxic effects at high levels. To make progress toward a single drug, Ruqaiyyah Siddiqui and colleagues turned to quinazolinones. These compounds are effective against a wide spectrum of human foes, including bacteria, viruses, fungi, parasites and cancer, but they had never been tested against brain-eating amoebae.

The researchers synthesized 34 new quinazolinone derivatives and studied their effects on *N. fowleri* and *B. mandrillaris*. Some of the new compounds were effective at killing the microorganisms and limiting the harm the pathogens could do to human cells in a Petri dish. In some cases, attaching silver nanoparticles to the derivatives enhanced that activity. The most effective compounds contained chlorine, methyl or methoxy groups, and their toxicity for human cells was low. The researchers say their results show that quinazolinones are good candidates for drug development studies.

More information: Mohammad Ridwane Mungroo et al, Aryl Quinazolinone Derivatives as Novel Therapeutic Agents against Brain-Eating Amoebae, *ACS Chemical Neuroscience* (2020). DOI: 10.1021/acschemneuro.9b00596