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Review

The cave microbiome as a source for drug discovery: Reality or pipe dream?

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ABSTRACT

This review highlights cave habitats, cave microbiomes and their potential for drug discovery. Such studies face many challenges, including access to remote and pristine caves, and sample collection and transport. Inappropriate physical and chemical growth conditions in the laboratory for the isolation and cultivation of cave microorganisms pose many complications including length of cultivation; some cave microorganisms can take weeks and even months to grow. Additionally, DNA extraction from cave environmental samples may be difficult due to the high concentration of various minerals that are natural DNA blocking agents. Once cave microorganisms are grown in the lab, other problems often arise, such as maintenance of pure culture, consistency of antimicrobial activity and fermentation conditions for antimicrobial production. In this review, we suggest that, although based on what has been done in the field, there is potential in using cave microorganisms to produce antimicrobial agents, one needs to be highly committed and prepared.

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1. Introduction

Today, diseases caused by infectious agents, particularly with multi-drug resistant properties, have become a major threat to public health around the world. Many approaches have been applied to solve this problem and diverse habitats, particularly extreme ones, have been explored to discover new, and more effective drugs against diseases that were once easily treated with existing antibiotics.

In this review, we describe cave habitats, and provide information on the characteristics that make them unique, including why they are considered extreme environments for certain forms of life. The cave microbiomes that have been studied so far are also described, and their biotechnological potentials elucidated. The challenges faced in using cave microorganisms to produce new drugs are acknowledged and some promising future directions in cave microbiology research are described.

Ultimately, this review is our attempt to suggest, based upon years of research findings from scientific communities around the world, that cave habitats and the microorganisms that live, adapt, survive and thrive in them, may likely be one of our next frontiers for the discovery of novel drugs.

2. Cave habitats

Cave habitats have been used by humans and animals for a very long time. Archeological studies have shown evidence of cave use even in the Paleolithic period. The reasons for humans to use caves are varied, including for shelter, storage, as sources of minerals, places for artistic expression, and as cultural, burial, and/or ceremonial sites. Today, on the other hand, human use of caves is restricted mainly to recreation and scientific exploration.

Caves have been studied for hundreds of years. A particularly interesting research endeavor, which tied biotechnology and microbiology together, was a classic study done in Lascaux Caves, in France. The goal in this case was to preserve the Paleolithic drawings and polychrome rock paintings created 17,000 years ago [1,2]. This artwork was threatened by the growth of algae, bacteria, and fungi that invaded following changes in the climate of the cave that were created when it was opened to tourists. There was considerable controversy about how best to preserve the paintings and who should study the fragile artwork. Although studies have continued since this troubling growth was discovered, no clear solution has been found for getting rid of the invaders without compromising the indigenous cave community [3]. This problem could likely be solved, however, if more knowledge of the species diversity and ecology of indigenous microbial communities was available. Genuine collaboration among artists, scientists and governments is necessary to understand and manage the impacts of human visitation on cave artefacts and ecosystems.

In his book, "Dark life: Martian nanobacteria, rock-eating cave bugs, and other extreme organisms of inner earth and outer space", the veteran caver Michael Taylor noted that life in the dark can be profoundly different from life in the light-and that it is interesting and diverse [4]. In fact, many are astounded by evidence of various forms of life thriving in such habitats; despite how dark they are, caves are far from devoid of life. In subsurface or subterranean habitats, the mechanisms of metabolism are unexpectedly different and diverse. Cave environments can be highly variable, unforgiving and threatening to life in many ways. Challenges include, limited availability of organic matter, variable levels of light and humidity, lack of/limited connectivity to the surface, low or high temperatures, the nature of the hydrological connection between the cave, the surface and the groundwater, exposure to human or other animal visitations, air flow and pressure conditions, and the types and concentration of minerals in the matrix of rock sur-