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Bacteria-Derived Chemotherapeutic Agents for Cancer Therapy: A Brief Overview

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ABSTRACT

Many antibiotics available at the clinic are natural products or derivatives of these products that originate from bacteria, fungi, plants, and animals. After the discovery of penicillin by Alexander Fleming in 1928, the discovery and extraction of antibiotics from natural sources expanded greatly. We can modify the chemical structure of natural antibiotics to improve their therapeutic efficiency or reduce their side effects. In recent decades, compounds have been extracted from bacteria that are the source of some important anticancer chemotherapy drugs for cancer management. In this article, some of these drugs are discussed.

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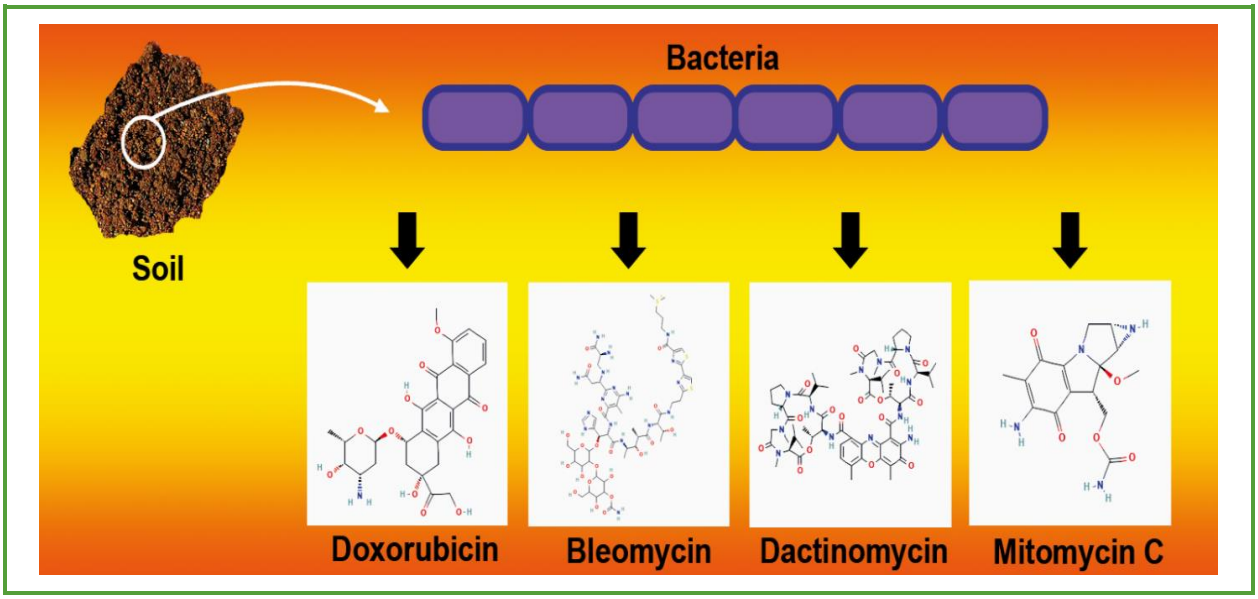
Graphical Abstract



Introduction

From the past thousands of years to today, the science of medicine and pharmacy has made significant progress. We have changed the use of natural products to extract pure medicinal compounds from these products and change the structure of these natural medicinal compounds or imitate them to make new medicinal compounds to treat diseases. With the progress in biomolecules separation techniques in the past decades, it has become possible to extract pure medicinal compounds from natural products for diseases treatment. In addition, after purifying medicinal compounds, it is possible to determine their chemical structure and modify them to improve efficiency or reduce side effects.

Alexander Fleming revolutionized the field of medicine by discovering and extracting penicillin from *Penicillium* mold in 1928 [1]. Today, many antibiotics in the market are natural products or derivatives of these products that originate from bacteria, fungi, plants, and animals. Soil bacteria have been a very rich source of antibiotics so that today 70-80% of antibiotics are derived from actinomycetes [2].

In recent decades, compounds have been extracted and purified from bacteria, which are the source of a number of important anticancer chemotherapy drugs for cancer management in the clinic (Figure 1). In this article, a brief overview of some of these chemotherapy drugs is presented originating from bacteria.

Doxorubicin

Doxorubicin is a drug from the anthracycline family, which is widely used in chemotherapy due to its effectiveness in fighting a wide range of cancers such as carcinoma, sarcoma, and blood cancers (Figure 2). The first two anthracyclines were isolated from the pigment-producing soil bacterium *Streptomyces peucetius* in the early 1960s and were named doxorubicin (DOX) and daunorubicin (DNR). The only difference between the two molecules is the fact that the side chain of DOX is terminated with a primary alcohol, while the side chain of DNR is terminated with a methyl group [3-5].

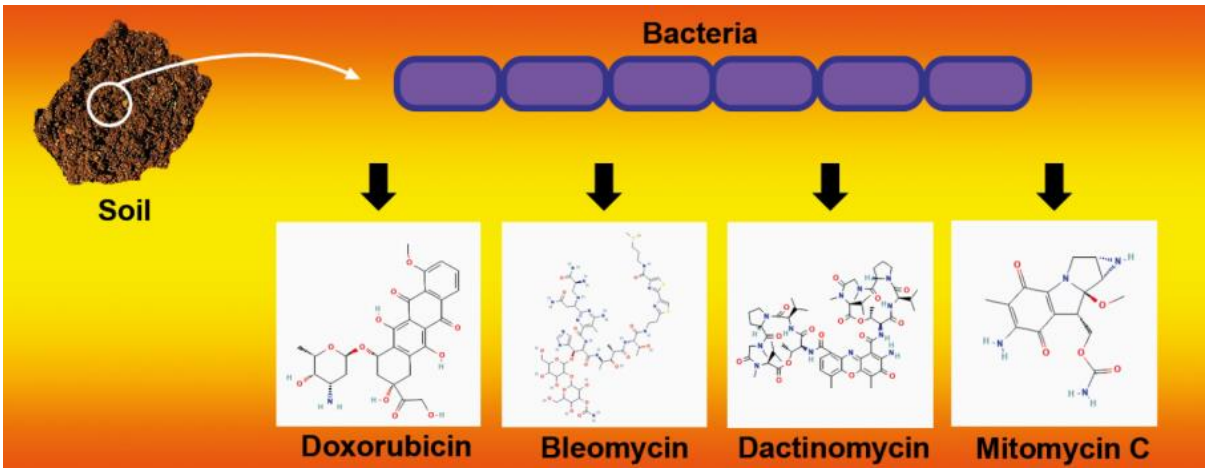


Figure 1. Bacteria-derived compounds which are among the important anticancer chemotherapy drugs for cancer management

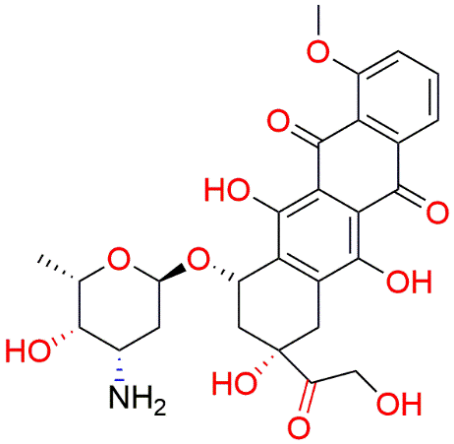


Figure 2. The chemical structure of doxorubicin. The 2D structure was derived from PubChem

Despite the widespread use of anthracyclines, their cytotoxic effects are multidirectional. Cardiotoxicity is the most well-known side effect of this group of drugs. To find a better anthracycline, about 2000 analogs have been produced with several chemical changes, substitutions, or conjugations. For example, epirubicin (EPI) is a semisynthetic derivative of DOX obtained from the axial-equatorial epimerization of hydroxyl group at the danosamine carbon. This change in position has little effect on the anticancer activity of EPI compared to DOX, but produces pharmacokinetic and metabolic changes such as increased volume of distribution, and thus increased the total body clearance of the drug or a final shorter half-life [4-6].

Bleomycin

Bleomycins were initially isolated from Gram-positive bacteria *Streptomyces verticillus* in Japan and their anticancer properties were studied (Figure 3) [7, 8]. Bleomycins are a family of glycopeptide antibiotics. Two types of bleomycins, bleomycin A2 and bleomycin A5, are used in the management of lymphomas (e.g., Hodgkin's lymphoma), head and neck cancer, and testicular cancer [9].

Dactinomycin

Dactinomycin or Actinomycin D was the first antibiotic whose anticancer effects were discovered (Figure 4). Actinomycin D is produced by various species of Actinomycetes mainly belonging to the genus *Streptomyces* [10]. Actinomycin D has the ability to inhibit transcription by binding to DNA in the transcription initiation complex and preventing RNA elongation by RNA polymerase [11]. Dactinomycin is used in the management of various solid tumors (nephroblastoma and sarcoma) [12].

Mitomycin C

Mitomycin C is a drug commonly used against several human malignancies such as gastrointestinal cancers, rectal cancer, breast cancer, and bladder cancer (Figure 5) [13]. This drug is produced by the bacteria *Streptomyces caespitosus* and is approved for the treatment of breast cancer, pancreatic cancer, non-small cell lung cancer, and the other cancers in combination with other chemotherapy agents. Mitomycin C exerts antitumor activity by cross-linking DNA.

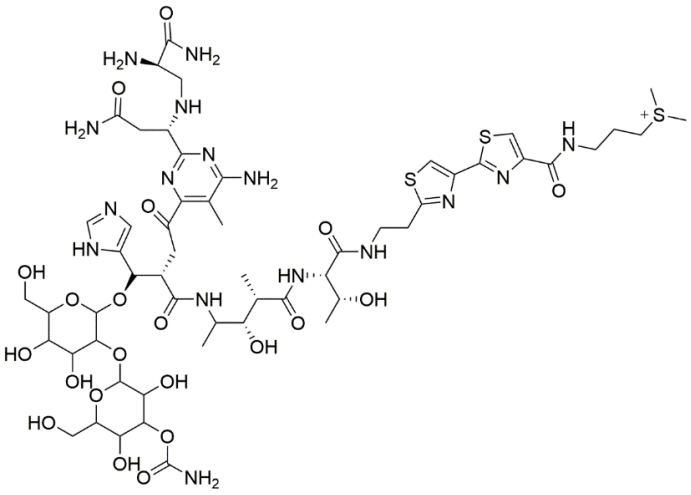


Figure 3. The chemical structure of bleomycin. The 2D structure was derived from PubChem

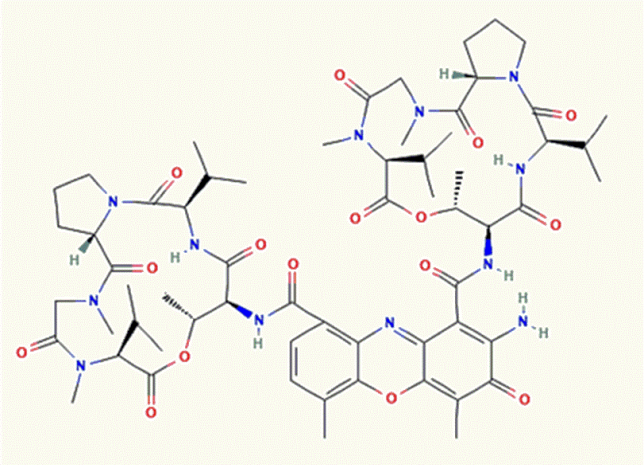


Figure 4. The chemical structure of dactinomycin. The 2D structure was derived from PubChem

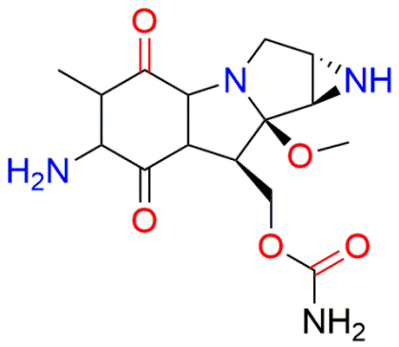


Figure 5. The chemical structure of mitomycin C. The 2D structure was derived from PubChem

Although mitomycin C is highly efficient as an anticancer agent, its clinical application has been significantly hampered by its toxicity to bone marrow and other tissues. Chemically, mitomycin C has quinone and aziridine moieties in its structure. The methylated derivative of mitomycin C called porphyromycin has shown significant therapeutic activity in combination with radiation therapy in head and neck cancer clinical trials [14].

Conclusion

Various compounds of bacteria have been discovered, extracted, and engineered that have been effective in treating cancer. Currently, some of these compounds such as doxorubicin, bleomycin, dactinomycin, and mitomycin C are used to treat various types of cancer in humans and are considered as one of the most important chemotherapy drugs for cancer.

Disclosure Statement

No potential conflict of interest was reported by the authors.

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Authors' Contributions

All authors contributed to data analysis, drafting, and revising of the paper and agreed to be responsible for all the aspects of this work.

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