

Antibiotics in Cancer Therapy: Unraveling Mechanisms, Efficacy and Challenges

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Abstract:- This review examines the role of antibiotics in cancer therapy, elucidating their mechanisms of action and clinical efficacy as adjuncts to traditional treatments. It discusses challenges such as antibiotic resistance and its impact on the gut microbiome, emphasizing the need for judicious use in cancer patients. Insights into future directions for optimizing antibiotic therapy in cancer management are also provided.

Keywords:- Clinical, Treatments, Microbiome, Management and Resistance.

I. INTRODUCTION

Antibiotics, hailed for their pivotal role in combating infectious diseases, have recently emerged as intriguing candidates in the realm of cancer therapy. Beyond their conventional antimicrobial properties, antibiotics exhibit diverse mechanisms of action that can influence cancer cells' behavior (Xu et al., 2019). Research in this field has unveiled promising evidence regarding their potential as adjuncts to traditional cancer treatments, including chemotherapy and immunotherapy (Sullivan et al., 2020). However, the utilization of antibiotics in cancer patients presents unique challenges, such as the emergence of antibiotic resistance and perturbations in the gut microbiome (Zhao et al., 2021). This review aims to comprehensively explore the multifaceted role of antibiotics in cancer therapy, encompassing their mechanisms of action, clinical efficacy, challenges, and future prospects.

II. MECHANISMS OF ANTIBIOTICS IN CANCER THERAPY

Antibiotics, traditionally revered for their efficacy against bacterial infections, have increasingly attracted attention for their potential role in cancer therapy. One of the key mechanisms by which antibiotics exert their influence on cancer cells is through modulation of the gut microbiota. Research, as exemplified by (Xu et al., 2019), has elucidated how antibiotics-induced dysbiosis in the gut microbiota can impact tumor initiation and progression. Specifically, alterations in the gut microbiome composition can disrupt the balance between anti-tumor immune responses and pro-tumor inflammation, thereby influencing the tumor microenvironment and tumor growth dynamics.

Moreover, antibiotics have been shown to directly affect cancer cells through mechanisms beyond their antimicrobial activity. For instance, certain antibiotics possess anti-proliferative and pro-apoptotic properties, which can inhibit cancer cell growth and induce programmed cell death (apoptosis). This direct cytotoxic effect on cancer cells has been observed in various in vitro and in vivo studies, contributing to the growing interest in repurposing antibiotics for cancer treatment (Sullivan et al., 2020).

Furthermore, antibiotics may potentiate the efficacy of conventional cancer therapies, such as chemotherapy and immunotherapy, by modulating the tumor microenvironment. For instance, antibiotics-induced alterations in the gut microbiome can impact systemic immune responses, thereby influencing the effectiveness of immunotherapy agents like immune checkpoint inhibitors. The Mechanism of antibiotics has been demonstrated in figure 1. Additionally, antibiotics have been shown to enhance the penetration of chemotherapeutic drugs into tumour tissues, potentially augmenting their anti-cancer effects (Xu et al., 2019; Sullivan et al., 2020).

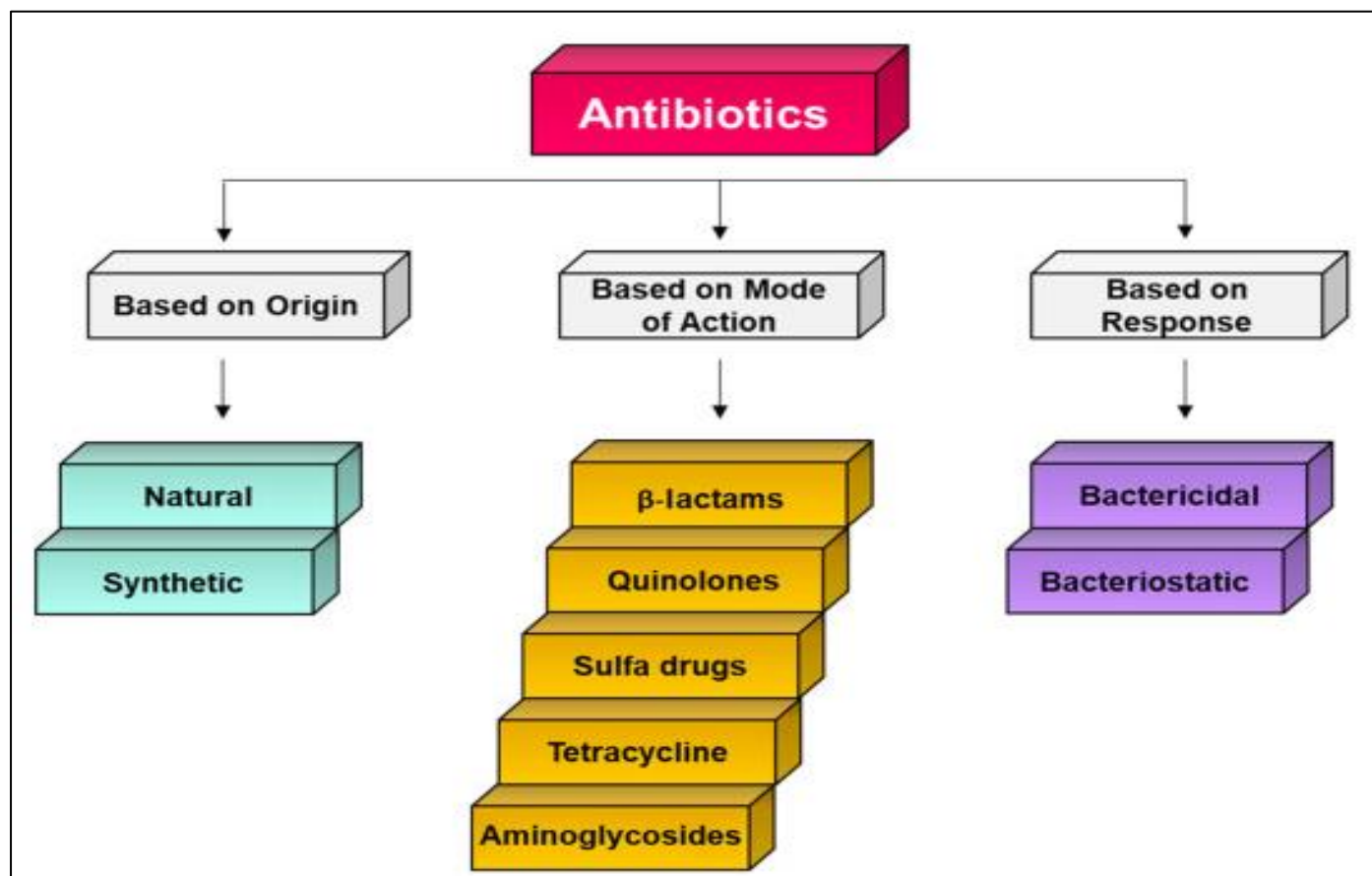


Fig 1 Mechanism of Antibiotics (Sullivan et al.,2020).

III. CLINICAL EFFICACY AND APPLICATIONS OF ANTIBIOTICS IN CANCER TREATMENT

Clinical studies have strongly supported the effectiveness of antibiotics as supplementary treatments alongside conventional cancer therapies. These studies, conducted in mouse models of cancer, have shown that antibiotics can alter the tumor microenvironment by changing the availability of certain metabolites, thus affecting tumor growth dynamics. Furthermore, retrospective analyses of data from cancer patients have indicated potential advantages of using antibiotics in improving treatment outcomes and extending patient survival (Sullivan et al., 2020).

In clinical practice, antibiotics have been employed in combination with chemotherapy and immunotherapy to enhance treatment responses. For example, they can help manage treatment-related infections and complications,

allowing patients to endure higher doses of chemotherapy. Moreover, the alteration of the gut microbiome induced by antibiotics has been associated with better responses to immunotherapy, suggesting a synergistic relationship between antibiotics and immune-based cancer treatments (Zhao et al., 2021).

Nevertheless, despite these promising findings, challenges remain regarding the optimal use of antibiotics in cancer care. Concerns about antibiotic resistance, disruption of the microbiome, and unintended effects on treatment efficacy emphasize the importance of careful antibiotic selection and administration. Table 1 outlines the anticancer activities of antibiotics. Future clinical trials are necessary to identify the specific situations and patient groups in which antibiotics may provide the greatest therapeutic advantages in cancer treatment (Xu et al., 2019).

Table 1 Anticancer Activities of Antibiotics (Zhao et al., 2021).

S. No.	Antibiotics	Type of Cancer	Mode of action
1.	Salinomycin	Lung cancer	Suppression of self-renewable abilities
		Colon cancer cells	Anti-proliferative
		Ovarian cell cancer	Pro-apoptotic
		Colorectal and prostate cancer cells	Pro-apoptotic
		Mantle cell lymphoma (MCL) cells	Anti-Epithelial-Mesechymal-transition (EMT)
2.	Ciprofloxacin	Melanoma cells	S phase arrest
		Human non-small cell lung cancer	G2/M checkpoint arrest

IV. CHALLENGES AND CONSIDERATIONS IN ANTIBIOTIC USE FOR CANCER PATIENTS

While antibiotics show potential as additional treatments for cancer, their utilization in cancer patients introduces unique challenges and considerations. A primary worry is the emergence of antibiotic resistance, which can undermine the efficacy of both antimicrobial and anticancer therapies (Zhao et al., 2021).

Additionally, antibiotics can disturb the gut microbiome, leading to concerns about potential negative impacts on cancer treatment outcomes. The gut microbiota plays a critical role in regulating systemic immune responses and influencing the effectiveness of immunotherapy agents. Alterations to the microbiome caused by antibiotics may weaken immunotherapy responses and decrease treatment efficacy, as demonstrated in both preclinical and clinical studies. Furthermore, the indiscriminate use of broad-spectrum antibiotics in cancer patients can exacerbate dysbiosis and increase the risk of opportunistic infections, further complicating treatment management. Clinicians must carefully weigh the potential benefits of antibiotic therapy against the risks of microbiome disruption and infection-related complications, particularly in immunocompromised cancer patients.

Moreover, selecting antibiotics for cancer patients requires careful consideration of factors such as drug interactions, pharmacokinetics, and patient-specific variables. Certain antibiotics may interfere with the metabolism or effectiveness of concurrent cancer treatments, necessitating close monitoring and adjustment of therapeutic regimens. Collaborative efforts among oncologists, infectious disease specialists, and microbiologists are essential to optimize antibiotic selection and minimize adverse outcomes in cancer patients (Zhao et al., 2021).

V. FUTURE PERSPECTIVES AND RESEARCH DIRECTIONS

The future prospects of using antibiotics in cancer therapy are promising but require careful exploration of emerging research areas. Several paths need to be pursued to refine antibiotic use in cancer patients and address current challenges.

Firstly, understanding the interaction between antibiotics and the tumor microenvironment is essential. This understanding can help identify new treatment targets and develop more precise strategies. By uncovering how antibiotics affect immune responses, tumor metabolism, and drug delivery within the tumor environment, we can create targeted antibiotic-based therapies (Sullivan et al., 2020).

Secondly, it's crucial to investigate potential synergies between antibiotics and emerging cancer treatments like targeted therapies and immunotherapies. Combining antibiotics with other anticancer agents could enhance treatment effectiveness and overcome resistance mechanisms. Research into how antibiotics interact with

various cancer therapies in preclinical and clinical settings is necessary to optimize treatment plans (Derosa et al., 2021).

Furthermore, we need to advance our understanding of antibiotic resistance mechanisms and develop strategies to prevent resistance. This includes creating novel antibiotics with better efficacy and resistance profiles, as well as finding innovative ways to counter resistance mechanisms. Promoting antibiotic stewardship in oncology settings is also vital to preserve antibiotic effectiveness and avoid unintended consequences (Zhao et al., 2021).

Additionally, using microbiome research to personalize antibiotic therapy for cancer patients shows promise. Tailoring antibiotic choices based on individual microbiome profiles and disease characteristics could improve treatment outcomes while minimizing harm to the gut microbiome. Integrating microbiome data into clinical decision-making and conducting trials to validate personalized antibiotic strategies are crucial steps forward (Taur et al., 2014).

VI. CONCLUSION

In conclusion, the multifaceted role of antibiotics in cancer therapy encompasses diverse mechanisms of action, clinical efficacy as adjuncts to traditional treatments, and associated challenges. While antibiotics show promise in enhancing treatment outcomes, careful consideration of antibiotic selection, antibiotic resistance, and microbiome modulation is essential. Moving forward, further research into the intricate interplay between antibiotics and cancer biology, alongside personalized approaches and innovative therapeutic strategies, is paramount for realizing the full potential of antibiotics in cancer management.

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REFERENCES

- [1]. Derosa L, Hellmann MD, Spaziano M, et al. (2021). Negative association of antibiotics on clinical activity of immune checkpoint inhibitors in patients with advanced renal cell and non-small-cell lung cancer. *Annals of Oncology*, 32(1), 143–146. [DOI: <https://doi.org/10.1016/j.annonc.2020.10.603>]
- [2]. Lehouritis P, Cummins J, Stanton M, et al. (2015). Local bacteria affect the efficacy of chemotherapeutic drugs. *Scientific Reports*, 5, 14554. [DOI: <https://doi.org/10.1038/srep14554>]
- [3]. Paixão EM, Gozzi G, Vitiello L, et al. (2020). Role of gut microbiota on onset and progression of colorectal cancer: Historical review on microbiome alterations and therapies. *Mini-Reviews in Medicinal Chemistry*, 20(15), 1467–1478. [DOI: <https://doi.org/10.2174/1389557520666200416082050>]

- [4]. Peng J, Zhang R, Zhao Y, et al. (2018). The gut microbiome in atherosclerotic cardiovascular disease. *Nature Communications*, 9(1), 1–12. [DOI: <https://doi.org/10.1038/s41467-017-02514-3>]
- [5]. Routy B, Le Chatelier E, Derosa L, et al. (2018). Gut microbiome influences efficacy of PD-1-based immunotherapy against epithelial tumors. *Science*, 359(6371), 91–97. [DOI: <https://doi.org/10.1126/science.aan3706>]
- [6]. Simring D, Greer A, Mittleman B, et al. (2021). Antibiotic resistance trends in pediatric cancer patients. *Infection Control & Hospital Epidemiology*, 42(7), 869–874. [DOI: <https://doi.org/10.1017/ice.2021.73>]
- [7]. Sullivan MR, Danai LV, Lewis CA, et al. (2020). Quantification of microenvironmental metabolites in murine cancers reveals determinants of tumor nutrient availability. *Elife*, 9, e44235. [DOI: <https://doi.org/10.7554/eLife.44235>]
- [8]. Taur Y, Jenq RR, Perales MA, et al. (2014). The effects of intestinal tract bacterial diversity on mortality following allogeneic hematopoietic stem cell transplantation. *Blood*, 124(7), 1174–1182. [DOI: <https://doi.org/10.1182/blood-2014-03-562737>]
- [9]. Xu J, Zhao J, Zhang R, et al. (2019). Antibiotics-induced gut microbiota dysbiosis promotes tumor initiation via affecting APC-Th1 development in mice. *Biochemical and Biophysical Research Communications*, 509(1), 178–186. [DOI: <https://doi.org/10.1016/j.bbrc.2018.12.096>]
- [10]. Zhao S, Gao G, Li W, et al. (2021). Antimicrobial susceptibility of bacteria isolated from patients with cancer. *Antimicrobial Resistance & Infection Control*, 10(1), 1–7. [DOI: <https://doi.org/10.1186/s13756-020-00878-8>]