

Natural Anthocyanins as Potential Antibacterial Agents: A Systematic Review

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Abstract

Anthocyanins are naturally occurring flavonoid pigments widely distributed in red, purple, and blue fruits and vegetables. In addition to their established antioxidant and anti-inflammatory properties, accumulating evidence suggests that anthocyanins possess considerable antibacterial potential. This systematic review aimed to critically evaluate the current scientific evidence regarding the antibacterial efficacy of anthocyanins. A comprehensive literature search was conducted using PubMed, ScienceDirect, ResearchGate, and Google Scholar to identify relevant in vitro studies published between 2020 and 2024. Study selection and data synthesis were performed in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines. A total of ten studies fulfilled the predefined inclusion criteria and were included in the final analysis. The findings demonstrated that anthocyanins isolated from various natural sources, including blueberries, sorghum, red cabbage, wild cabbage, red radish peels, and black chokeberry, exhibited significant antibacterial activity against both Gram-positive and Gram-negative bacterial pathogens. The antibacterial mechanisms of anthocyanins were primarily attributed to disruption of bacterial cell membrane integrity, inhibition of biofilm formation, and interference with essential metabolic pathways. Nevertheless, further mechanistic investigations are required to elucidate the molecular basis underlying these antibacterial effects. Overall, the available evidence indicates that anthocyanins are promising natural antibacterial agents and may serve as potential candidates for the development of novel therapeutic strategies to combat the escalating global challenge of antibiotic resistance.

Keywords: Anthocyanins, Antibacterial, Natural source, Alternative therapy

Abstrak

Potensi Antosianin Alami sebagai Agen Antibakteri: Tinjauan Sistematis. Antosianin merupakan pigmen flavonoid alami yang tersebar luas pada berbagai buah dan sayuran berwarna merah, ungu, dan biru. Selain memiliki aktivitas antioksidan dan antiinflamasi yang telah banyak dilaporkan, bukti ilmiah yang terus berkembang menunjukkan bahwa antosianin juga memiliki potensi sebagai agen antibakteri. Tinjauan sistematis ini bertujuan untuk mengevaluasi secara kritis bukti ilmiah terkini mengenai efektivitas antibakteri antosianin. Penelusuran literatur dilakukan secara komprehensif melalui basis data PubMed, ScienceDirect, ResearchGate, dan Google Scholar untuk mengidentifikasi penelitian in vitro yang relevan dan dipublikasikan pada periode 2020–2024. Seleksi studi dan sintesis data dilakukan sesuai dengan pedoman Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA). Sebanyak sepuluh penelitian memenuhi kriteria inklusi yang telah ditetapkan dan selanjutnya dianalisis dalam tinjauan ini. Hasil kajian menunjukkan bahwa antosianin yang diisolasi dari berbagai sumber alami, seperti blueberry, sorgum, kubis merah, kubis liar, kulit lobak merah, dan black chokeberry, memiliki aktivitas antibakteri yang signifikan terhadap bakteri patogen Gram-positif maupun Gram-negatif. Mekanisme kerja antibakteri antosianin terutama meliputi gangguan terhadap integritas membran sel bakteri, penghambatan pembentukan biofilm, serta interferensi terhadap jalur metabolisme esensial bakteri. Meskipun demikian, penelitian lebih lanjut masih diperlukan untuk mengungkap mekanisme molekuler yang mendasari aktivitas antibakteri tersebut.

Secara keseluruhan, bukti ilmiah yang tersedia menunjukkan bahwa antosianin merupakan senyawa antibakteri alami yang menjanjikan dan berpotensi dikembangkan sebagai kandidat terapi baru dalam menghadapi tantangan global berupa meningkatnya resistensi antibiotik.

Kata Kunci: *Antosianin, Antibakteri, Sumber alami, Terapi alternatif*

Introduction

Anthocyanins are nature-derived pigments present in various purple, red, and blue fruits and vegetables, including blueberries, shorgum, red cabbage, wild cabbage, red radish peels, and black chokeberry. Anthocyanins belong to a group of naturally occurring, water-soluble pigments classified under the flavonoid family. They are quite common in nature and can be found in the roots, stems, tubers, leaves, fruits, seeds, and colored petals of flowers.¹ Anthocyanins can be classified as secondary metabolites and polyphenols because due to their structural core, which consists of a 2-phenylbenzopyrylium unit, also known as a flavylium cation.²

Beyond their biological roles as antioxidants and anti-inflammatory agents, anthocyanins have attracted attention as potential antibacterial agents.³ The urgency for novel therapeutic alternatives is heightened by the rise in global antibiotic resistance, leading to treatment failures for bacterial infections and elevated morbidity and mortality rates.⁴ In 2019, antimicrobial resistance was associated with approximately 4.95 million deaths, including 1.27 million fatalities directly attributable to it.⁵

Previous studies have shown that anthocyanins can inhibit the growth of various human pathogenic bacteria, including *Staphylococcus aureus*, *Escherichia coli*, and *Salmonella* sp.^{6,7} The antibacterial activity of anthocyanins is believed to be related to their ability to decrease cellular metabolism in biofilms, decreased biofilm thickness, disrupt the integrity of the cell wall and membrane, leading to the leakage of cellular proteins.⁸⁻¹⁰

However, although the antibacterial potential of anthocyanins has been reported in various in vitro studies, there is still a knowledge gap regarding the molecular mechanisms underlying these effects and their application in clinical medicine. This systematic review aims to collect and analyze the existing scientific evidence regarding the antibacterial activity of anthocyanins from various natural sources. By evaluating the existing literature, this review is expected to provide further insight into the potential applications of anthocyanins as natural antibacterial agents and identify areas that require further research.

Methods

Literature Search Strategy

This study was conducted as a systematic literature review following the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines to ensure a transparent and reproducible study selection process. A comprehensive literature search was performed in four electronic databases, namely PubMed, ScienceDirect, ResearchGate, and Google Scholar. The search included articles published between January 2020 and December 2024. The following keywords and Boolean operators were used: ("anthocyanins" OR "anthocyanin") AND ("antibacterial" OR "antimicrobial") AND ("natural agents" OR "natural source" OR "alternative therapy").

Eligibility Criteria

Studies were included if they met the following criteria: (1) original in vitro research articles; (2) evaluated the antibacterial activity of anthocyanins derived from natural sources; (3) reported antibacterial testing methods and outcomes; and (4) were published in English. Review articles, conference abstracts,

editorials, case reports, animal studies, clinical studies, and publications with insufficient methodological information were excluded.

Study Selection

All retrieved articles were screened through title and abstract evaluation, followed by full-text assessment based on the predefined inclusion and exclusion criteria. Duplicate articles were removed before the screening process. The study selection process was documented using a PRISMA flow diagram (Figure 1).

Data Extraction and Analysis

Relevant data from the eligible studies were extracted using a standardized data collection form. The extracted information included the source of anthocyanins, extraction or preparation methods (when available), bacterial species tested, antibacterial assay methods (including disc diffusion, broth microdilution, minimum inhibitory concentration (MIC), minimum bactericidal concentration (MBC), and synergistic assays), major findings, and proposed antibacterial mechanisms. The extracted data were analyzed descriptively and synthesized qualitatively to compare antibacterial efficacy among different anthocyanin sources.

Quality Assessment

The methodological quality of the included studies was evaluated based on the clarity of experimental design, description of anthocyanin sources, antibacterial testing procedures, reproducibility of the methods, and completeness of the reported results. Studies with inadequate methodological descriptions or insufficient outcome data were excluded from the final analysis.

Results and Discussion

This systematic review summarizes current evidence regarding the antibacterial activity of anthocyanins derived from natural sources. Ten eligible *in vitro* studies published between 2020 and 2024 were included after a systematic screening process based on the PRISMA guidelines. The included studies evaluated various anthocyanin-rich extracts against clinically important Gram-positive and Gram-negative bacteria using different antibacterial assays. The results of this systematic review indicate that anthocyanins, natural pigments found in various fruits and vegetables, have potential as effective antibacterial agents. The various *in vitro* studies evaluated in this review consistently reported antibacterial activity of anthocyanins against several important pathogenic bacteria, including *Staphylococcus aureus*, *Escherichia coli*, *Pseudomonas aeruginosa*, *Klebsiella pneumoniae*, *Acinetobacter baumannii*, *Salmonella enteritidis*, *Salmonella enterica*, etc. These findings support the hypothesis that anthocyanins can inhibit bacterial growth through several mechanisms of action, such as cell membrane damage, inhibition of biofilm formation, and influence on bacterial metabolic enzyme activities.^{11,12}

Study Selection

The study selection process began with a literature search that resulted in a total of 160 articles from PubMed, ScienceDirect, and Google Scholar. After elimination of duplicates and initial assessment based on titles and abstracts, a total of 85 articles remained. Furthermore, 75 articles which did not fulfill the criteria of inclusion were excluded. From these, 10 studies satisfied the criteria of inclusion and were thoroughly analyzed in this review.

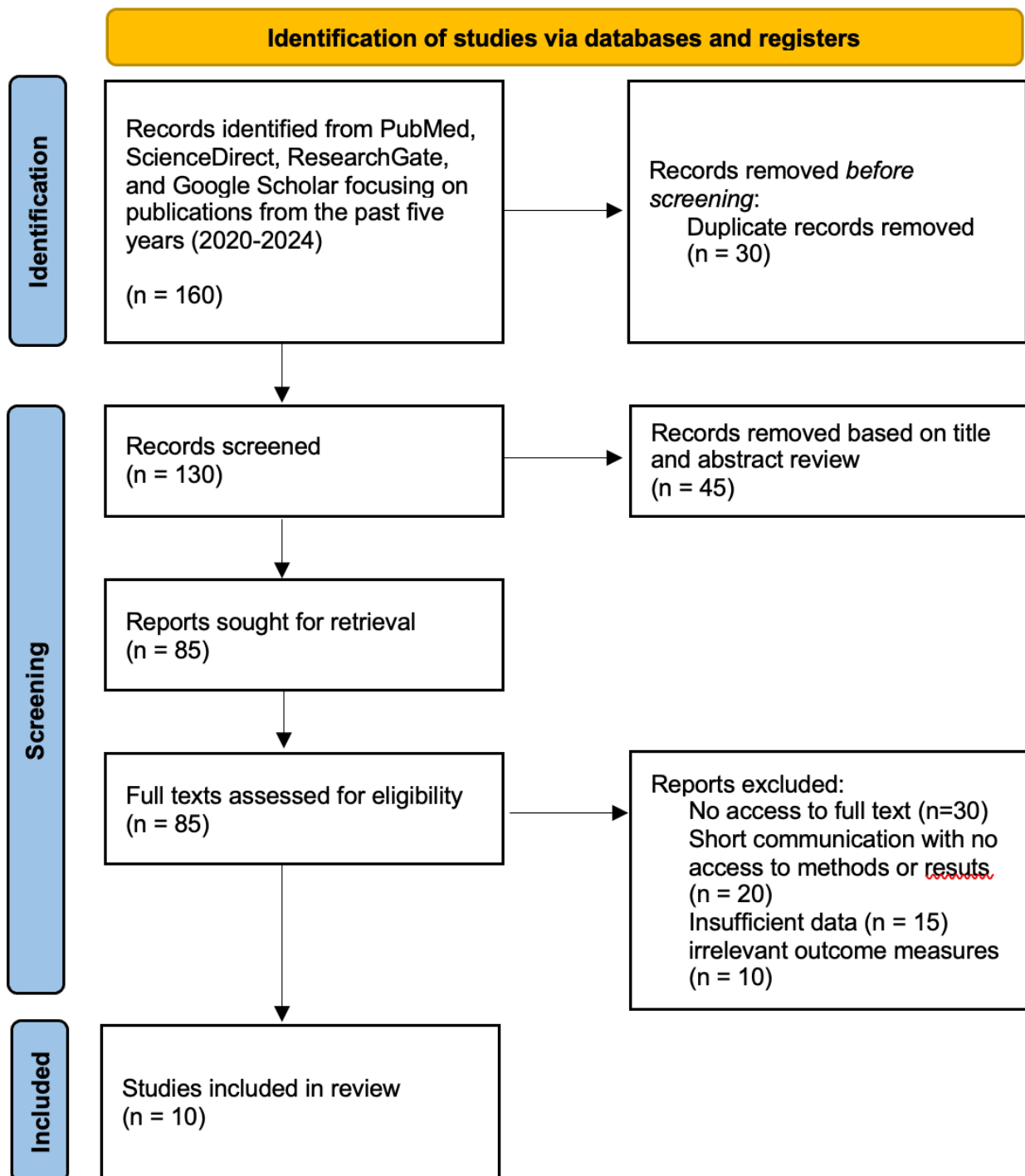


Figure 1. PRISMA flow diagram of the screening and selection process

Study Characteristics

The studies included in this review were from numerous nature-derived sources of anthocyanins. All studies were conducted under in vitro laboratory conditions. Antibacterial test methods used included disc diffusion tests, microbial dilution tests. The types of bacteria tested include *Staphylococcus aureus*, *Escherichia*

coli, *Pseudomonas aeruginosa*, *Klebsiella pneumoniae*, *Acinetobacter baumannii*, *Salmonella enteritidis*, *Salmonella enterica*, etc.

Mechanisms of Antibacterial Action

Way of working of anthocyanins in inhibiting bacterial growth seems to be related to their chemical properties that are able to damage the integrity of bacterial cell membranes. Anthocyanins can disrupt bacterial cell membranes, causing leakage of intracellular contents, which leads to bacterial cell death. For example, *Aronia melanocarpa* anthocyanins were shown to destroy the cell membrane of *E. coli* O157 and similar effects were seen with anthocyanins from *Lycium ruihenicum* Murr on *S. aureus*.^{23,24} Furthermore, the capacity of anthocyanins to impede bacterial protein synthesis and biofilm formation are an important finding considering that biofilm is one of the main defense strategies of bacteria against conventional antibiotics.²⁴ By inhibiting biofilms, anthocyanins not only reduce the ability of bacteria to survive in unfavorable environments, but also increase their susceptibility to other antibacterial therapies. *Lycium ruthenicum* Murr anthocyanins, for example, inhibited protein synthesis in *S. aureus* and disrupted biofilm.²⁴

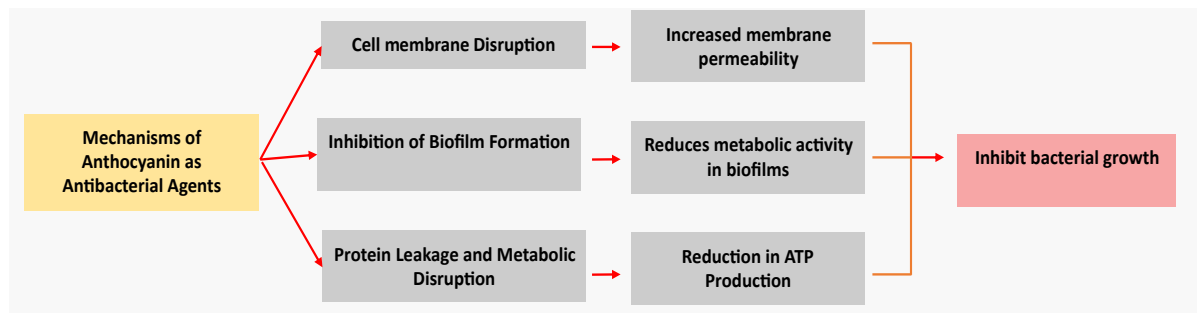


Figure 2. Mechanisms of Anthocyanin as Antibacterial Agents

The variety of antibacterial mechanisms exhibited by anthocyanins is illustrated in this diagram (Figure 2). These compounds disrupt the integrity of bacterial membranes, causing leakage of intracellular components and disrupting homeostasis. They also induce oxidative stress by increasing the production of reactive oxygen species (ROS), leading to damage to proteins, lipids and nucleic acids (Figure 3). Anthocyanins further inhibit key metabolic processes, including protein synthesis, fatty acid biosynthesis, and nucleic acid production, which impairs bacterial growth and function. In addition, they interfere with glycolysis, pyruvate metabolism, and the tricarboxylic acid (TCA) cycle, reducing energy production. Disruption of amino acid metabolism also limits the adaptability of bacteria. Collectively, these mechanisms weaken bacterial defenses, inhibit biofilm formation, and increase susceptibility to external antibacterial agents.²⁵

Clinical Implications and Future Perspectives

While in vitro results demonstrate the strong antibacterial potential of anthocyanins, it is important to note that clinical data supporting their use in clinical settings is limited. The studies included in this review were generally conducted under controlled laboratory conditions, which may not fully reflect conditions in the human body. Therefore, more in vivo research and clinical trials are required to confirm not only the effectiveness but also safety of anthocyanins as antibacterial agents in clinical settings. In addition, variations in extraction methods, types of bacteria tested, and anthocyanin formulations used in different studies are factors to consider when interpreting these results. This variability may affect the potency of antibacterial activity and make it difficult to conclude strong and general conclusions about the effectiveness of anthocyanins as antibacterial agents.

Table 1. Characteristics of the included studies.

Author (Year of Publication)	Title	Method	Anthocyanin Sources	Bacterial agent	Result
Cerezo <i>et al</i> (2020) ¹³	Anthocyanins in Blueberries Grown in Hot Climate Exert Strong Antioxidant Activity and May Be Effective against Urinary Tract Bacteria	MIC	Blueberry (<i>Vaccinium corymbosum</i>)	<i>Klebsiella pneumoniae</i> , <i>Providencia stuartii</i> and <i>Micrococcus spp.</i> strains isolated from UTI	The extracts inhibited all the tested strains, MICs ranging from 0.4 mg/mL (for Stella Blue extract against UTI <i>P. aeruginosa</i>) to 9.5 mg/mL (for all extracts against UTI <i>K. pneumoniae ssp. pneumoniae</i>).
Dong <i>et al</i> (2022) ¹⁴	Antibacterial effect and mechanism of anthocyanin from <i>Lycium ruthenicum</i> Murr	MIC; Growth inhibition assay, biofilm assay, SEM for structural changes in biofilm	Pang Ma (<i>Lycium ruthenicum</i> Murr)	<i>Staphylococcus aureus</i> (S. aureus), <i>Escherichia coli</i> (E. coli), <i>Aspergillus niger</i> and <i>Penicillium sp.</i>	Inhibited bacterial growth and biofilm formation; disrupted cell membrane integrity and affected protein synthesis.
Jeyaraj <i>et al</i> (2023) ¹⁵	Metabolic perturbations and key pathways associated with the bacteriostatic activity of <i>Clitoria ternatea</i> flower anthocyanin fraction against <i>Escherichia coli</i>	Time kill assay	Butterfly pea flower (<i>Clitoria ternatea</i>)	<i>Escherichia coli</i> ATCC 25922	Reduced bacterial growth by 95.8% (MIC) and 99.9% (2× MIC); perturbed key metabolic pathways involved in cell function.
Deng <i>et al</i> (2022) ¹⁶	Proteomic analyses revealed the antibacterial mechanism of <i>Aronia melanocarpa</i> isolated anthocyanins against <i>Escherichia coli</i> O157: H7	TMT proteomics and ROS detection to study the antibacterial mechanism	Chokeberry (<i>Aronia melanocarpa</i>)	<i>Escherichia coli</i> O157: H7	Disrupts cell membrane, increases intracellular ROS, affects carbohydrate, amino acid, and lipid metabolism.
Silva <i>et al</i> (2023) ¹⁷	Selective Activity of an Anthocyanin-Rich, Purified Blueberry Extract upon Pathogenic and Probiotic Bacterial	Inhibition assay at different concentrations (1000 µg/mL) on pathogenic and probiotic bacteria, and metabolic assessment	Blueberry extract	<i>Escherichia coli</i> NCTC 9001, <i>Salmonella enteritidis</i> ATCC 13076, <i>Listeria monocytogenes</i> ESB 3562, and <i>Bacillus cereus</i> NCTC 2599	Inhibits pathogen growth, no effect on probiotics' growth but enhances organic acid production in probiotics.

Liu et al (2021) ¹⁸	Enhancement on Antioxidant and Antibacterial Activities of Brightwell Blueberry by Extraction and Purification	Disk diffusion assay	Brightwell Blueberry	<i>Listeria monocytogenes</i> (21,532), <i>Salmonella enterica</i> (ATCC 51,812), and <i>Escherichia coli</i> (ATCC 25,922).	Brightwell blueberry extract has antibacterial activity against <i>E. coli</i> (16.04 ± 0.38) and <i>S. enterica</i> (10.95 ± 0.64), but no inhibition zone for <i>Listeria monocytogenes</i> .
Salamon, et al (2021) ¹⁹	Antiproliferative and Antimicrobial Activity of Anthocyanins from Berry Fruits after Their Isolation and Freeze-Drying	Agar diffusion test and Serial Dilutions	High-bush blueberry, <i>Vaccinium corymbosum</i> L., Bilberry, <i>Vaccinium myrtillus</i> L., Elderberry, <i>Sambucus nigra</i> L. Black Chokeberry, <i>Aronia melanocarpa</i> Wild.	<i>Candida albicans</i> ATCC 885-653; <i>Staphylococcus aureus</i> ATCC 25923; <i>Escherichia coli</i> ATCC 25922; <i>Enterococcus faecalis</i> ATCC 29212; <i>Streptococcus pyogenes</i> ATCC 19615.	It was determined that the anthocyanin content in the extracts obtained by the freeze-drying method was acceptable, and some extracts were found to have a strong antiproliferative effect on colorectal cancer cells and have an antibacterial effect on typical and clinical strains.
Suganyadevi et al (2020) ²⁰	Antimicrobial Activity of Anthocyanins Extracted from Red Shorgum (<i>Shorgum bicolor</i> .L) Bran	Agar –well diffusion for determination of antibacterial activity	<i>Sorghum</i> (<i>Sorghum bicolor</i> (L))	<i>Escherichia coli</i> , <i>Klebsiella oxytoca</i> , <i>Klebsiella pneumonia</i> , <i>Pseudomonas aeruginosa</i> , <i>Staphylococcus aureus</i>	In all four Gram negative bacterias the methanol extract of anthocyanin showed no inhibitory zone even at 12.5 mg concentrations. For <i>Staphylococcus aureus</i> , the zone of inhibition values of anthocyanin extracts were between 5-9 mm.
Abdullah and Mohammed (2024) ²¹	The Study of the Antibacterial Effect of Anthocyanin Pigment Extracted from Red Cabbage (<i>Brassica oleracea</i> var. <i>capitata</i> f. <i>rubra</i>) and Red Radish Peels (<i>Raphanus sativus</i> . var. <i>sativus</i>)	Agar well diffusion	Red Cabbage (<i>Brassica oleracea</i> var. <i>capitata</i> f. <i>rubra</i>) and Red Radish (<i>Raphanus sativus</i> . var. <i>sativus</i>)	<i>Staphylococcus epidermidis</i> and <i>Acinetobacter baumannii</i>	The results of both cabbage and radish anthocyanin extracts on <i>S.epidermidis</i> and <i>A.baumannii</i> showed positive antibacterial effect with wide range of differences which is

								increasing directly in proportion with anthocyanin extract concentrations for both cabbage and radish. Significant inhibition with higher anthocyanin concentrations: up to 39 mm (<i>S. epidermidis</i>), 33 mm (<i>A. baumannii</i>)
Tallam et al (2023) ²²	Evaluation of antibacterial property of anthocyanin extracted from brassica oleracea against gram positive and gram negative bacteria by using erythromycin as a standard drug	Agar disc diffusion: Minimum Inhibitory Concentration (MIC)	Cabbage (<i>Brassica oleracea</i>)	<i>Escherichia coli</i> and <i>Lactobacilli acidophilus</i> .				The results of <i>Brassica oleracea</i> anthocyanin extracts on <i>E. coli</i> and <i>L. acidophilus</i> showed positive antibacterial effect compared to standard erythromycin with zone of inhibition 20.83 mm against <i>E. coli</i> and 15.56 mm against <i>Bacillus</i> .

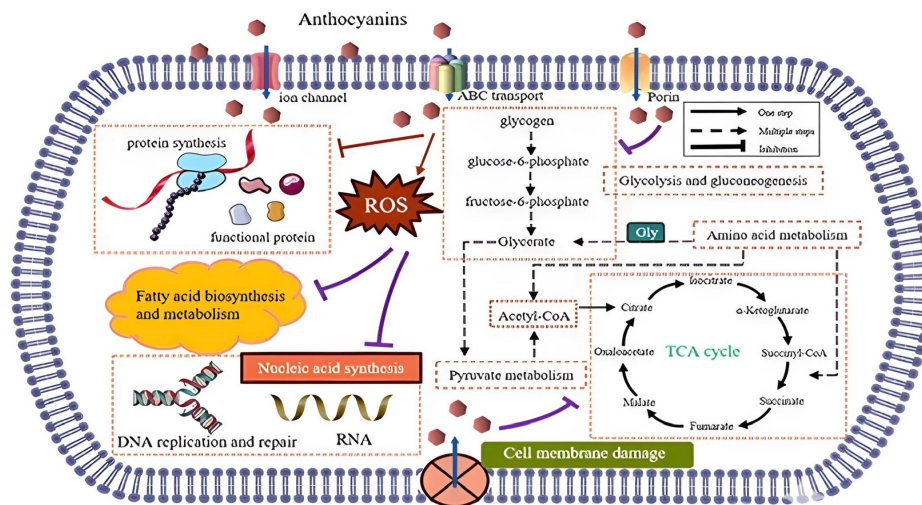


Figure 3. Antibacterial mechanism of anthocyanins via membrane disruption, ROS induction.²⁵

Based on the discoveries above, a few suggestions and recommendations for upcoming research can be proposed. First, further studies should explore the effects of anthocyanins against a wider variety of pathogenic bacteria, including antibiotic-resistant bacteria. Second, research should be focused on determining the optimal dose, formulation, and method of use of anthocyanins for clinical applications. Third, it is important to conduct research on the molecular mechanisms underlying the synergistic effect between anthocyanins and antibiotics, which may pave the way for the development of more effective antibacterial therapeutic combinations. Finally, research should consider the potential toxicity and side effects of anthocyanins to ensure their safety on long-term use.

Conclusions

This systematic review evaluates the potential of anthocyanins as natural antibacterial agents. Analysis of multiple *in vitro* studies revealed that anthocyanins derived from diverse natural sources can inhibit the growth of various bacterial pathogens through different mechanisms of action. This study answers the hypothesis that anthocyanins have significant antibacterial effects and can serve as an alternative to antibiotic therapy, especially in the context of increasing antibiotic resistance. These findings are in accordance with the objectives of the study which aimed to identify the role of anthocyanins as potential antimicrobial agents.

Future research should focus on *in vivo* research and clinical trials to confirm the effectiveness and safety of anthocyanins in humans. In addition, further research is needed to understand the molecular mechanisms underlying the antibacterial activity of anthocyanins and explore potential synergists with conventional antibiotics. These studies should also consider optimal formulations and delivery methods of anthocyanins for clinical applications. These attempts will help develop new strategies in antibacterial therapy and overcome the global antibiotic resistance challenge.

Conflict of Interest

The authors declare that there is no conflict of interest regarding the publication of this study.

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