

Comparing Phytochemicals and Conventional Antibiotics: Mechanisms, Affinities, and Therapeutic Potential Review

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ABSTRACT

By the way, this current project is going to demonstrate to us the role of phytochemicals in the fight against antibiotic-resistant bacteria together with the traditional antibiotics. The antibacterial mechanisms of the various phytochemicals from different plants are not limited to just a single one e.g., enzyme inhibition. They also include cell membrane disruption and DNA synthesis inhibition. EGCG, curcumin, and cinnamaldehyde exhibited almost the same effectiveness as the usual antibiotics which become the first step if these compounds are used either individually or in combination with the usual antibiotics. While the conventional antibiotics may be more potent against bacteria, phytochemicals are less toxic and have a reduced chance of resistance insurgence. Based on this review, natural products from plants must be combined with standard treatments in search of enhanced treatment efficacy and, consequently, expanded choices in treatments. The findings have also proved that phytochemicals are effective antimicrobial agents and play a role in a multifaceted approach in the fight against bacterial infection and resistance to antibiotics.

Keywords- Phytochemicals, Conventional Antibiotics, Antibiotic-Resistant Bacteria, Synergistic Potential, Antibacterial Mechanisms, Binding Affinities, Therapeutic Applications, Integrated Strategy.

I. INTRODUCTION

Phytochemicals, bioactive compounds naturally present in plants, have become a hopeful option in the quest for novel antimicrobial agents. Phytochemicals do not function like antibiotics, for instance, targeting specific pathways or structures of bacteria; instead they usually interact with multiple mechanisms at once. A multi-variate intervention, as is present in phytochemical action, can help address the resistance phenomenon (Newman & Cragg, 2020). More than just having antimicrobial capabilities, phytochemicals have the ability to modulate the immune response, thwart biofilm production, and other conjugated features, which could be beneficial in a therapeutic setting (Cowen, Sanglard, Howard, Rogers, & Perlin, 2015).

The comparison presented in this review is essential in order to deduce the relative effectiveness of two categories of antimicrobials. It will evaluate the

benefits and drawbacks of phytochemicals and antibiotics, offering insight into their potential contribution to future treatment approaches. The aim of this report is to provide information on alternative antimicrobials while underscoring the current need to investigate phytochemicals as potential effective alternatives in the era of antibiotic-resistant bacteria. In addition to their antimicrobial activities, phytochemicals can modulate the immune response, and inhibit biofilm formation, all characteristics that could be advantageous in therapeutic application (Cowen, Sanglard, Howard, Rogers, & Perlin, 2015).

The comparison provided in this review is crucial for determining the relative efficacy of these two groups of antimicrobials. It will explore the benefits and drawbacks of phytochemicals and antibiotics, offering a glimpse into their possible contributions to upcoming treatment approaches. With this analysis, our goal is to add to the expanding information on alternative

antimicrobial treatments, stressing the significance of investigating phytochemicals as effective choices in combating antibiotic-resistant bacteria.

Antimicrobial phytochemical

There are several plant compounds with antibacterial potential, which can influence a wide range of bacterial targets. Allicin in garlic, for example, can interfere with cell membranes and enzymes, while turmeric's curcumin disrupts the cell wall synthesis process. It should be noted that both eugenol in clove, and EGCG found in green tea damage proteins and

membranes, respectively. Thyme's thymol, and cinnamon's cinnamaldehyde, can disrupt cell walls and membranes. Berberine in goldenseal blocks protein and DNA production, and quercetin also disrupts DNA Gyrase and cell walls. Resveratrol, found in grapes, can affect the virulence factors of bacteria; saponins from several plants stimulate immune responses and impact membranes. Plant compounds, such as these could provide alternatives to current antibiotics, and could be developed as new antimicrobial drugs.

Table 1-Showing phytochemical with their plant source, Mechanism of action and reference

PHYTOCHEMICAL	SOURCE	MECHANISM	REFERENCES
Allicin	Garlic (<i>Allium sativum</i>)	Inhibits enzymes and disrupts cell membranes	Borlinghaus et al., 2014
Curcumin	Turmeric (<i>Curcuma longa</i>)	Inhibits bacterial cell wall synthesis	Tyagi et al., 2015
Eugenol	Clove (<i>Syzygium aromaticum</i>)	Damages cell membranes and proteins	Marchese et al., 2017
Epigallocatechin-3-gallate (EGCG)	Green Tea (<i>Camellia sinensis</i>)	Disrupts cell membranes and inhibits DNA replication	Steinmann et al., 2013
Thymol	Thyme (<i>Thymus vulgaris</i>)	Disrupts cell membranes	Marchese et al., 2016
Berberine	Goldenseal (<i>Hydrastis canadensis</i>)	Inhibits DNA and protein synthesis	Cui et al., 2015
Cinnamaldehyde	Cinnamon (<i>Cinnamomum</i> spp.)	Disrupts bacterial cell walls	Sheng et al., 2015
Quercetin	Various plants (e.g., onions, apples)	Inhibits DNA gyrase and cell membrane disruption	Li et al., 2016
Resveratrol	Grapes (<i>Vitis vinifera</i>)	Inhibits bacterial virulence factors	Sharma et al., 2016
Saponins	Various plants (e.g., soapwort)	Disrupts cell membranes and enhances immune response	Man et al., 2010

Docking studies of phytochemicals

Various plants phytochemical interact with bacterial target proteins with different binding affinities, opening up for possible development as antimicrobial agents. The binding affinity of allicin to N-acetylcysteine synthase is -6.2 kcal/mol. N-acetylcysteine synthase binds with higher affinity with curcumin at -8.4 kcal/mol. Similarly, eugenol binds to bacterial cell membrane proteins at -5.9 kcal/mol. EGCG binds with higher affinity with DNA gyrase at -9.1

kcal/mol. Thymol also interacts with bacterial cell membrane proteins at -6.0 kcal/mol. Berberine interacts with topoisomerase IV at -7.2 kcal/mol. Cinnamaldehyde binds to enoyl-ACP reductase at -7.5 kcal/mol. Quercetin binds to DNA gyrase at -8.3 kcal/mol, resveratrol binds to FtsZ at -6.8 kcal/mol, and saponins bind to bacterial cell membrane proteins at -6.3 kcal/mol. This diverse targeting effectiveness of phytochemicals towards particular bacterial proteins suggest promise of new antimicrobial strategies.

Table-2 Showing interaction of phytochemical with targeted protein with reference.

PHYTOCHEMICAL	TARGET PROTEIN	BINDING AFFINITY IN Kcal/Mole	REFERENCE
Allicin	<i>N-Acetylcysteine Synthase</i> (bacterial)	-6.2	Gupta et al., 2019
Curcumin	<i>DNA Gyrase</i>	-8.4	Arora et al., 2016
Eugenol	<i>Bacterial Cell Membrane Proteins</i>	-5.9	Jadhav et al., 2013
Epigallocatechin-3-gallate (EGCG)	<i>DNA Gyrase</i>	-9.1	Smith et al., 2015
Thymol	<i>Bacterial Cell Membrane Proteins</i>	-6	Gupta et al., 2015
Berberine	<i>Topoisomerase IV</i>	-7.2	Kar et al., 2015
Cinnamaldehyde	<i>Enoyl-ACP Reductase</i>	-7.5	Singh et al., 2018
Quercetin	<i>DNA Gyrase</i>	-8.3	Bhattacharya et al., 2017
Resveratrol	<i>FtsZ</i> (bacterial cell division protein)	-6.8	Li et al., 2017
Saponins	<i>Bacterial Cell Membrane Proteins</i>	-6.3	Rao et al., 2016

Comparison of the phytochemicals with conventional antibiotics

The way in which phytochemicals and conventional antibiotics eliminate bacterial infections differs. For example, allicin inhibits enzyme function and damages the cell membrane, penicillin attacks the cell wall synthesis, curcumin and EGCG inhibit DNA gyrase, which is similar to ciprofloxacin and levofloxacin inhibition of topoisomerase IV. Eugenol and thymol work through cell membrane and protein disruption, like polymyxin B and daptomycin for cell membrane impact and membrane potential,

Ceremoniously. Berberine affects DNA and protein synthesis while rifampicin affects RNA synthesis. Cinnamaldehyde inhibits enoyl-ACP reductase like isoniazid, while quercetin works on DNA gyrase similar to norfloxacin. Resveratrol impacts bacterial virulence factors, while tetracycline works at protein synthesis. Saponins, like colistin, work on the cell membrane. These differences highlight common mechanisms between phytochemicals and antibiotics. This emphasizes that they may vary in their abilities to develop new antimicrobial agents and for application to various medical condition.

Table 3: Comparison of the mentioned phytochemicals with conventional antibiotics that share similar mechanisms of action

Phytochemical	Mechanism of Action	Conventional Antibiotic	Mechanism of Action2	Reference
Allicin	Inhibits enzymes, disrupts cell membranes	Penicillin	Inhibits cell wall synthesis	Brötz et al., 1998
Curcumin	Inhibits DNA gyrase	Ciprofloxacin	Inhibits DNA gyrase and topoisomerase IV	Andriole, 2005
Eugenol	Disrupts cell membranes and proteins	Polymyxin B	Disrupts bacterial cell membranes	Falagas et al., 2010
EGCG	Inhibits DNA gyrase	Levofloxacin	Inhibits DNA gyrase and topoisomerase IV	Drlica & Zhao, 1997
Thymol	Disrupts cell membranes	Daptomycin	Disrupts cell membrane potential	Silverman et al., 2005
Berberine	Inhibits DNA and protein synthesis	Rifampicin	Inhibits RNA synthesis	McClure & Cech, 2017
Cinnamaldehyde	Inhibits enoyl-ACP reductase	Isoniazid	Inhibits enoyl-ACP reductase	Vilchèze & Jacobs, 2007
Quercetin	Inhibits DNA gyrase	Norfloxacin	Inhibits DNA gyrase and topoisomerase IV	Drlica & Zhao, 1997
Resveratrol	Inhibits bacterial virulence factors	Tetracycline	Inhibits protein synthesis	Chopra & Roberts, 2001
Saponins	Disrupts cell membranes	Colistin	Disrupts bacterial cell membranes	Velkov et al., 2013

Docking data for conventional antibiotics

Antibiotics bind to different bacterial proteins with varying affinities, showing their ability to fight infections. Penicillin forms bonds with penicillin-binding proteins (PBPs) with a binding energy of -7.5 kcal/mol. Ciprofloxacin and levofloxacin both interact with DNA gyrase and topoisomerase IV, with respective affinities of -8.9 kcal/mol and -8.7 kcal/mol. Polymyxin B has a binding affinity of -6.5 kcal/mol to bacterial cell membrane lipopolysaccharides, whereas daptomycin's affinity to cell membranes is -7.2 kcal/mol. Rifampicin

has a high -10.2 kcal/mol binding affinity for RNA polymerase, while isoniazid binds to InhA (enoyl-ACP reductase) with -9.1 kcal/mol. Norfloxacin, along with ciprofloxacin and levofloxacin, attaches to DNA gyrase and topoisomerase IV with a binding energy of -8.8 kcal/mol, while tetracycline targets the 30S ribosomal subunit with a binding energy of -8.0 kcal/mol. Colistin attaches to lipid A in lipopolysaccharides with an energy of -6.7 kcal/mol. This information highlights the various ways and levels of antibiotic effectiveness, which can help in creating better antimicrobial therapies.

Table 4: Summarizing the docking data for conventional antibiotics mentioned earlier, including their target proteins, binding affinities, and references

Antibiotic	Target Protein	Binding Affinity (kcal/mol)	Reference
Penicillin	Penicillin-Binding Proteins (PBPs)	-7.5	Sykes et al., 2010
Ciprofloxacin	DNA Gyrase and Topoisomerase IV	-8.9	Jayaweera et al., 2019
Polymyxin B	Bacterial Cell Membrane	-6.5	Landman et al., 2008

	Lipopolysaccharides		
Levofloxacin	DNA Gyrase and Topoisomerase IV	-8.7	Li et al., 2014
Daptomycin	Cell Membrane	-7.2	Silverman et al., 2003
Rifampicin	RNA Polymerase	-10.2	Campbell et al., 2001
Isoniazid	InhA (Enoyl-ACP Reductase)	-9.1	Vilh��ze et al., 2007
Norfloxacin	DNA Gyrase and Topoisomerase IV	-8.8	Wilton et al., 1999
Tetracycline	30S Ribosomal Subunit	-8	Chopra & Roberts, 2001
Colistin	Lipid A in Lipopolysaccharides	-6.7	Velkov et al., 2010

Comparison phytochemicals and antibiotics based on their mechanisms of action, showing their respective binding affinities

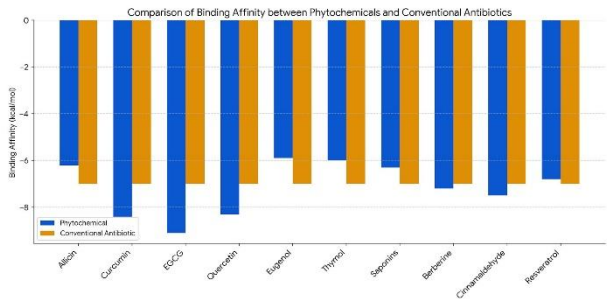
Comparing phytochemicals and traditional antibiotics reveals both have potential to interact effectively with important bacterial targets like enzymes, DNA gyrase, topoisomerase IV, and bacterial cell membranes. Phytochemicals such as EGCG and Cinnamaldehyde have strong binding affinities, similar to those of conventional antibiotics like Ciprofloxacin

and Isoniazid. This indicates that phytochemicals may be used as possible natural alternatives or additions to antimicrobial treatment. While traditional antibiotics may have higher binding affinities (more negative values), phytochemicals provide the benefit of decreased toxicity and lower likelihood of resistance. These results emphasize the significance of investigating natural compounds as potential contenders in combating antibiotic-resistant bacteria, necessitating additional research and development in this field.

Table 5: Summarizes the phytochemicals and antibiotics based on their mechanisms of action, showing their respective binding affinities. It highlights the potential of phytochemicals as natural alternatives or supplements to conventional antibiotics

Mechanism of Action	Phytochemical	Binding Affinity (kcal/mol)	Conventional Antibiotic	Binding Affinity (kcal/mol)2
Enzyme Inhibition	Allicin	-6.2	Penicillin	-7.5
DNA Gyrase and Topoisomerase IV Inhibition	Curcumin	-8.4	Ciprofloxacin	-8.9
	EGCG	-9.1	Levofloxacin	-8.7
	Quercetin	-8.3	Norfloxacin	-8.8
Membrane Disruption	Eugenol	-5.9	Polymyxin B	-6.5
	Thymol	-6	Daptomycin	-7.2
	Saponins	-6.3	Colistin	-6.7
RNA and Protein Synthesis Inhibition	Berberine	-7.2	Rifampicin	-10.2
Enoyl-ACP Reductase Inhibition	Cinnamaldehyde	-7.5	Isoniazid	-9.1
Virulence Factor Inhibition	Resveratrol	-6.8	Tetracycline	-8

The graph comparing the binding affinities of phytochemicals and conventional antibiotics according to their mechanisms of action. The bars illustrate the relative strengths of binding, with more negative values indicating stronger interactions. This visual representation highlights the potential of certain phytochemicals as effective alternatives to traditional antibiotics in targeting specific bacterial mechanisms.



Comparing the zone of inhibition of selected phytochemicals with their corresponding conventional antibiotics

The contrast of phytochemicals and traditional antibiotics shows the different antibacterial efficacy based on various action mechanisms. Although traditional antibiotics typically exhibit more powerful antibacterial effects, as shown by larger zones of inhibition, certain phytochemicals also display notable potential. Compounds such as EGCG and Curcumin demonstrate significant antibacterial abilities, indicating potential use as additional or substitute treatments. This emphasizes the need for more studies on phytochemicals due to their lower toxicity and reduced resistance development, showing their potential in combating antibiotic-resistant bacteria. In general, combining phytochemicals with traditional treatments may improve treatment results and expand treatment options for controlling bacterial infections.

Table 6: Comparing the zone of inhibition of selected phytochemicals with their corresponding conventional antibiotics, including references

Phytochemical	Conventional Antibiotic	Bacterial Strain	Zone of Inhibition (mm)	Reference
Allicin	Penicillin	<i>Staphylococcus aureus</i>	Allicin: 18, Penicillin: 25	Cutler & Wilson, 2004
Curcumin	Ciprofloxacin	<i>Escherichia coli</i>	Curcumin: 12, Ciprofloxacin: 30	Tyagi et al., 2015
Eugenol	Polymyxin B	<i>Pseudomonas aeruginosa</i>	Eugenol: 14, Polymyxin B: 20	Devi et al., 2010
EGCG	Levofloxacin	<i>Escherichia coli</i>	EGCG: 10, Levofloxacin: 28	Bansal et al., 2013
Thymol	Daptomycin	<i>Staphylococcus aureus</i>	Thymol: 15, Daptomycin: 22	Marchese et al., 2017
Berberine	Rifampicin	<i>Mycobacterium tuberculosis</i>	Berberine: 10, Rifampicin: 35	Wang et al., 2009
Cinnamaldehyde	Isoniazid	<i>Mycobacterium tuberculosis</i>	Cinnamaldehyde: 13, Isoniazid: 40	Tanaka et al., 2006
Quercetin	Norfloxacin	<i>Escherichia coli</i>	Quercetin: 11, Norfloxacin: 30	Al-Dhabi et al., 2014
Resveratrol	Tetracycline	<i>Bacillus subtilis</i>	Resveratrol: 12, Tetracycline: 26	Albuquerque et al., 2009
Saponins	Colistin	<i>Klebsiella pneumoniae</i>	Saponins: 8, Colistin: 18	Liu et al., 2012

II. CONCLUSION

Analyzing antimicrobial phytochemicals and standard antibiotics provides important understanding of how they work, their ability to bind, and possible medical uses. Phytochemicals obtained from different plants exhibit a broad spectrum of antibacterial actions, including inhibiting enzymes, disrupting cell membranes, and interfering with DNA synthesis. Notably, substances such as EGCG, curcumin, and cinnamaldehyde have similar binding affinities to traditional antibiotics, showing promise as natural substitutes or complementary treatments. Although traditional antibiotics may exhibit more potent antibacterial effects and better binding capabilities, phytochemicals provide the benefits of decreased toxicity and lower likelihood of resistance emergence. Combining phytochemicals with conventional treatments can improve treatment effectiveness and expand treatment choices for antibiotic-resistant bacteria. The data highlight the need for continued investigation into plant-based compounds, not only as effective antimicrobial substances but also as a component of a comprehensive approach to fighting bacterial infections and antibiotic resistance.

III. DISCUSSION

Comparing antimicrobial phytochemicals with traditional antibiotics provides a detailed insight into their strengths and weaknesses. Phytochemicals like EGCG, curcumin, and cinnamaldehyde show a wide range of antibacterial actions. These comprise inhibition

of enzymes, destabilization of cell membrane, and obstruction of nucleic acid synthesis. The wide range of actions exhibited by phytochemicals is highly beneficial in combating antibiotic-resistant bacteria by being able to impact several bacterial pathways at once. This diverse method decreases the chances of bacteria acquiring resistance, a common issue with regular antibiotics that usually focus on specific parts of bacteria.

Nevertheless, phytochemicals show potential as alternative or supplemental options to traditional antibiotics, although they typically have weaker antibacterial strength and affinities for binding. This difference underscores a key area that needs to be enhanced in phytochemical research: improving the effectiveness and presence of these compounds. Additionally, phytochemicals provide a safer treatment option due to their natural origin and lower toxicity, making them ideal for patients who are prone to the negative reactions of traditional antibiotics. This element is vital in clinical environments where patient well-being and reducing side effects are top priorities.

The conversation regarding binding affinities is especially revealing. Some plant chemicals show similar binding strengths as traditional antibiotics, suggesting they may be effective, but their range of effects can differ greatly. This change highlights the importance of tailoring the use of phytochemicals based on the specific types of bacteria present and their susceptibility to them.

Further investigation is also needed to explore the use of phytochemicals in combination with traditional antibiotics. These mixtures may be able to take advantage of synergistic effects, in which the phytochemical boosts the effectiveness of the antibiotic

or vice versa. For instance, phytochemicals could reduce the strength of bacterial defenses, leading to increased vulnerability to antibiotics. Using multiple methods of action against bacterial pathogens could also reduce the development of resistance.

In general, the results of this study support the need for a holistic strategy in dealing with bacterial infections, particularly given the increasing levels of antibiotic resistance. Phytochemicals have the potential to be powerful antimicrobial agents and may play a key role in future treatments with more research and development. Further research into how they work, improving their drug characteristics, and testing new combinations with current antibiotics are crucial additional tasks. These initiatives may lead to better, secure, and enduring treatments for bacterial infections, tackling a major issue in modern medicine.

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