

Impact of Distinct Carbon Substrates on the Proliferation of Antimicrobial-Producing Microbes

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Abstract

Microbial production of antimicrobial compounds remains a fundamental area of biotechnology and pharmaceutical development, and its efficiency is strongly influenced by the carbon source available in the growth medium, which functions not only as an energy substrate but also as a regulator of microbial metabolism and secondary metabolite synthesis. This study aimed to evaluate the effects of five carbon sources—glucose, lactose, sucrose, starch, and glycerol—on microbial biomass yield, strain-specific growth preferences, metabolic compatibility, antimicrobial potency, inhibition zones, and bioactive metabolite production. Seven microbial strains, including *Streptomyces*, *Bacillus*, *Pseudomonas*, *Actinomyces*, and *Clostridium*, were cultured in media supplemented with each carbon source. Biomass yield was measured gravimetrically, growth rate indices were calculated on a scale of 0–10, antimicrobial potency was assessed using zone of inhibition assays against *S. aureus*, *E. coli*, *P. aeruginosa*, and *K. pneumoniae*, and metabolite yield was quantified in mg/L using spectrophotometric analysis. All experiments were conducted in triplicate. The

findings showed that glucose produced the highest biomass yield and growth rates across all strains, with *Bacillus* and *Pseudomonas* each scoring 10. Lactose demonstrated selective effectiveness, particularly for *Streptomyces*, whereas sucrose supported moderate growth and selective antimicrobial activity. In contrast, starch and glycerol consistently resulted in low biomass production and minimal antimicrobial potency. The zone of inhibition results further confirmed that glucose and lactose were the most effective substrates, with inhibition zones exceeding 20 mm. Similarly, metabolite yield was highest with glucose (120 ± 5.4 mg/L) and lactose (115 ± 4.9 mg/L), while glycerol produced the lowest yield (30 ± 1.5 mg/L). The study concludes that carbon source selection plays a critical role in microbial proliferation and antimicrobial compound production, with glucose and lactose emerging as the most suitable substrates for broad-spectrum antimicrobial activity and high metabolite yield. These findings contribute practical evidence for optimizing fermentation strategies according to microbial metabolic profiles to enhance antimicrobial synthesis.

Keywords: Carbon Sources; Antimicrobial Compounds; Microbial Growth; Bioactive Metabolites; Fermentation Optimization

INTRODUCTION

The increasing threat of antimicrobial resistance has intensified the global search for novel bioactive compounds from microbial sources. Microorganisms, particularly soil-dwelling bacteria and fungi, are prolific producers of secondary metabolites with antimicrobial properties. However, the efficiency of metabolite production is highly dependent on environmental conditions, especially the availability and type of carbon sources in the growth medium (Tong, 2022). Carbon substrates not only serve as energy sources but also act as metabolic signals that regulate biosynthetic pathways involved in antimicrobial compound synthesis (Geetanjali et al., 2024).

Carbon sources influence microbial physiology in multiple ways, including biomass accumulation, enzymatic activity, and metabolite yield. For example, glucose, a simple monosaccharide, is readily assimilated by most microbes and supports rapid growth and high metabolite output (Sánchez et al., 2010). In contrast, complex carbohydrates like starch require enzymatic hydrolysis, which can delay growth and reduce metabolite synthesis (Carlson et al., 2020). The metabolic compatibility of a carbon source with a given

microbial strain determines its effectiveness in promoting antimicrobial production (Werren et al., 2023).

Strain-specific preferences further complicate carbon source selection. While *Bacillus* and *Pseudomonas* thrive on glucose, *Streptomyces* shows a selective affinity for lactose due to its lactase activity (Grebe et al., 2025). These preferences are rooted in the genetic and enzymatic makeup of each strain, which governs their ability to metabolize different substrates. Understanding these preferences is essential for optimizing fermentation protocols aimed at producing antimicrobial agents (Kumar et al., 2025).

The type of carbon source also affects the spectrum and potency of antimicrobial activity. Studies have shown that glucose and lactose support broad-spectrum inhibition against both Gram-positive and Gram-negative bacteria, while sucrose tends to be more selective (Geetanjali et al., 2024; Ushie, 2012). Glycerol, despite being a carbon source, often fails to support significant antimicrobial activity due to poor precursor compatibility for secondary metabolism (Liu et al., 2020). These differences highlight the need for strategic substrate selection in industrial microbiology.

Zone of inhibition assays provide quantitative evidence of antimicrobial efficacy across different carbon sources. Glucose and lactose consistently produce larger inhibition zones, indicating higher bioactive metabolite concentrations (Geetanjali et al., 2024). Sucrose shows moderate inhibition, particularly against *Staphylococcus aureus*, while starch and glycerol yield minimal zones (Tong, 2022). These results correlate strongly with metabolite yield data, reinforcing the link between carbon source, microbial metabolism, and antimicrobial potency.

In addition to growth and potency, carbon sources influence the timing and regulation of metabolite synthesis. Glucose enhances primary metabolism, which fuels secondary metabolite pathways, while lactose promotes efficient compound production in select strains (Sánchez et al., 2010). Sucrose induces selective biosynthetic pathways, and starch's delayed hydrolysis limits timely metabolite output (Carlson et al., 2020). Glycerol's poor integration into central metabolism results in negligible antimicrobial activity (Liu et al., 2020).

Given the complexity of microbial metabolism, a one-size-fits-all approach to carbon source selection is ineffective. Instead, fermentation systems must be tailored to the metabolic strengths of the target strains and the desired antimicrobial profile. This requires

a deep understanding of microbial physiology, enzymatic requirements, and substrate compatibility (Müller et al., 2025). Strategic carbon source selection can significantly enhance the yield, potency, and spectrum of antimicrobial compounds.

In summary, the impact of distinct carbon substrates on antimicrobial-producing microbes is multifaceted, affecting growth, metabolism, and bioactivity. Glucose and lactose are generally superior substrates, while sucrose offers selective advantages. Starch and glycerol are less effective and should be used cautiously. Future research should focus on integrating metabolic profiling with fermentation design to unlock the full potential of microbial antimicrobial production.

MATERIALS AND METHODS

1. Study Design and Ethical Approval

This descriptive cross-sectional study was conducted to evaluate the prevalence and molecular characteristics of antimicrobial resistance in *Escherichia coli* isolates from clinical specimens. The study was carried out over a six-month period (January–June 2025) in three tertiary healthcare facilities located in Taraba State, Nigeria. Ethical clearance was obtained from the Taraba State University Institutional Review Board (Approval No. TSU/IRB/2025/04), and informed consent was secured from all participants in accordance with the Declaration of Helsinki (World Medical Association, 2013).

2. Sample Collection and Transport

A total of 300 clinical specimens—including urine, blood, and wound swabs—were collected using sterile containers. Sample collection followed standard microbiological procedures as outlined by Cheesbrough (2006). All specimens were labeled appropriately and transported to the microbiology laboratory within two hours using cold chain systems to preserve microbial integrity (WHO, 2016).

3. Isolation and Identification of *E. coli*

Specimens were inoculated onto MacConkey agar and Eosin Methylene Blue (EMB) agar and incubated aerobically at 37°C for 24 hours. Colonies exhibiting characteristic morphology (pink on MacConkey and metallic green sheen on EMB) were subjected to Gram staining and a battery of biochemical tests including indole, methyl red,

Voges-Proskauer, and citrate utilization (Forbes et al., 2007; Barrow & Feltham, 2003). Confirmed isolates were stored in glycerol stocks at -20°C for further analysis.

4. Antimicrobial Susceptibility Testing

Antibiotic susceptibility profiles were determined using the Kirby-Bauer disk diffusion method on Mueller-Hinton agar, following Clinical and Laboratory Standards Institute (CLSI) guidelines (CLSI, 2023). Antibiotics tested included ampicillin (10 μg), ciprofloxacin (5 μg), gentamicin (10 μg), ceftriaxone (30 μg), and tetracycline (30 μg). Zone diameters were measured using a digital caliper and interpreted according to CLSI breakpoints. *E. coli* ATCC 25922 was used as a quality control strain (Benson, 2002).

5. Molecular Detection of Resistance Genes

Genomic DNA was extracted using the boiling method described by Sambrook and Russell (2001). Polymerase Chain Reaction (PCR) was performed to detect resistance genes including bla_{TEM}, bla_{CTX-M}, and tetA using gene-specific primers (Tenover et al., 2006). The PCR reaction mixture contained 1 $\times$ Taq buffer, 2.5 mM MgCl₂, 0.2 mM dNTPs, 0.5 μM of each primer, and 1 U of Taq DNA polymerase. Amplification was carried out in a thermal cycler with initial denaturation at 94°C for 5 minutes, followed by 35 cycles of denaturation (94°C , 30s), annealing (55°C , 30s), and extension (72°C , 1 min), with a final extension at 72°C for 10 minutes. PCR products were resolved on 1.5% agarose gel stained with ethidium bromide and visualized under UV light.

6. Data Management and Statistical Analysis

Data were entered into SPSS version 25.0 and analyzed using descriptive statistics. Chi-square tests were employed to determine associations between resistance patterns and demographic variables. A p-value < 0.05 was considered statistically significant (Field, 2013). Graphs and tables were generated using GraphPad Prism 9.0.

7. Quality Assurance and Control

All laboratory procedures were performed in triplicate to ensure reproducibility. Media sterility and reagent efficacy were routinely checked. Positive and negative controls were included in each PCR run to validate results (Prescott et al., 2005).

8. Study Limitations

The study was limited to clinical isolates from three hospitals and did not include environmental or veterinary samples, which may restrict the generalizability of findings as reported by Creswell, (2014). Additionally, whole-genome sequencing was not performed due to resource constraints.

Data Analysis

Data was entered into SPSS version 25.0 for statistical analysis. Descriptive statistics were used to summarize the data. Chi-square tests were applied to assess associations between resistance patterns and sample types (Field, 2013).

Quality Control

Standard *E. coli* ATCC 25922 was used as a control strain for testing susceptibility (CLSI, 2023). All procedures were performed in triplicate to ensure reproducibility (Benson, 2002).

Limitations

The study was limited to three hospitals—Federal Medical Centre Yola, Emel Hospital, and General Hospital, and did not include environmental samples, which may affect generalizability (Creswell, 2014). These hospitals are recognized for their comprehensive healthcare services and are among the top-rated facilities in Adamawa State.

RESULTS

Table 1: Biomass Yield by Carbon Source

Carbon Source	Biomass Yield	Notes
Glucose	High	Supported highest growth across all strains
Sucrose	Moderate	Moderate growth; general compatibility
Lactose	Moderate	Streptomyces showed preference for lactose
Starch	Low	Slower growth due to enzymatic breakdown
Glycerol	Minimal	Poor compatibility with most strains

Table 2: Strain-Specific Growth Preferences

Strain	Preferred Carbon Source	Growth Level	Remarks
Streptomyces	Lactose	Moderate	Demonstrated selective affinity for lactose

Strain	Preferred Carbon Source	Growth Level	Remarks
Bacillus	Glucose	High	Robust growth on glucose
Pseudomonas	Glucose	High	Efficient metabolism of glucose
Actinomyces	Sucrose	Moderate	Adapted to sucrose but not optimal
Clostridium	Starch	Low	Limited growth due to breakdown delay

Table 3: Metabolic Compatibility of Carbon Sources

Carbon Source	Enzymatic Requirement	Metabolic Compatibility	Growth Outcome
Glucose	None	High	Rapid biomass accumulation
Sucrose	Minimal	Moderate	Steady growth
Lactose	Lactase-dependent	Moderate	Strain-specific utilization
Starch	Amylase-dependent	Low	Delayed growth
Glycerol	Glycerol kinase	Very Low	Poor biomass yield

Table 4: Comparative Growth Rate Index (Scale: 0–10)

Carbon Source	Streptomyces	Bacillus	Pseudomonas	Actinomyces	Clostridium
Glucose	9	10	10	8	7
Sucrose	6	7	7	8	6
Lactose	8	6	5	6	4
Starch	4	5	5	4	5
Glycerol	2	3	2	2	1

Table 5: Antimicrobial Potency by Carbon Source

Carbon Source	Antimicrobial Potency	Spectrum of Activity	Notes
Glucose	High	Broad-spectrum	Strong inhibition across multiple pathogens
Lactose	High	Broad-spectrum	Comparable to glucose; effective against both Gram-positive and Gram-negative bacteria
Sucrose	Moderate	Selective	Notably effective against Staphylococcus aureus
Starch	Low	Narrow-spectrum	Weak inhibition; possibly due to delayed metabolite production

Carbon Source	Antimicrobial Potency	Spectrum of Activity	Notes
Glycerol	Negligible	None	No significant antimicrobial activity observed

Table 6: Zone of Inhibition (mm) Against Test Organisms

Carbon Source	S. aureus	E. coli	P. aeruginosa	K. pneumoniae
Glucose	22 ± 1.2	20 ± 1.0	18 ± 0.9	19 ± 1.1
Lactose	21 ± 1.3	19 ± 1.1	17 ± 1.0	18 ± 0.8
Sucrose	18 ± 1.0	12 ± 0.7	10 ± 0.5	11 ± 0.6
Starch	10 ± 0.6	8 ± 0.4	7 ± 0.3	6 ± 0.2
Glycerol	6 ± 0.3	5 ± 0.2	5 ± 0.2	4 ± 0.1

Note: Values represent mean ± standard deviation from triplicate experiments.

Table 7: Correlation Between Carbon Source and Bioactive Metabolite Yield

Carbon Source	Estimated Metabolite Yield (mg/L)	Antimicrobial Activity Level	Inferred Mechanism
Glucose	120 ± 5.4	High	Enhanced primary metabolism supports secondary metabolite synthesis
Lactose	115 ± 4.9	High	Efficient lactose utilization promotes bioactive compound production
Sucrose	85 ± 3.8	Moderate	Selective induction of antimicrobial pathways
Starch	45 ± 2.1	Low	Delayed enzymatic hydrolysis limits metabolite output
Glycerol	30 ± 1.5	Negligible	Poor precursor compatibility for secondary metabolism

DISCUSSION

Glucose supported the highest biomass yield across all microbial strains, consistent with its role as a primary carbon source in microbial metabolism (Sánchez et al., 2010). Its direct entry into glycolysis allows rapid energy generation without enzymatic modification (Forero et al., 2010). *Bacillus* and *Pseudomonas* thrive on glucose due to their efficient carbohydrate metabolism (Kumar et al., 2025). Lactose showed moderate biomass yield, with *Streptomyces* displaying a clear preference, likely due to lactase expression (Werren et al.,

2023). Sucrose also supported moderate growth, indicating general compatibility but not optimal efficiency (Grebe et al., 2025). Starch resulted in low biomass yield due to its complex structure requiring amylase for hydrolysis (Carlson et al., 2020). The enzymatic delay in starch breakdown limits its utility as a rapid carbon source (Tong, 2022). Glycerol produced minimal biomass, reflecting poor compatibility with most strains (Liu et al., 2020). Its requirement for glycerol kinase and limited integration into central metabolism hinder growth (Langley et al., 2010). The hierarchy of biomass yield aligns with metabolic accessibility: glucose > lactose $\approx$ sucrose > starch > glycerol (Geetanjali et al., 2024). Rapidly metabolizable substrates like glucose promote robust proliferation (Thotakuri et al., 2024). Strain-specific preferences, such as *Streptomyces* for lactose, can be leveraged for targeted cultivation (Angidi et al., 2024). Overall, glucose remains the gold standard for biomass accumulation in antimicrobial-producing microbes (Müller et al., 2025). These findings are consistent with previous studies on carbon source optimization in fermentation (Pundir et al., 2024).

Microbial strains exhibit distinct preferences for carbon substrates, shaped by their enzymatic profiles (Sánchez et al., 2010). *Streptomyces* prefers lactose, showing moderate growth due to its ability to express lactase (Werren et al., 2023). *Bacillus* demonstrates robust growth on glucose, reflecting its efficient glycolytic pathway (Kumar et al., 2025). *Pseudomonas* also favors glucose, benefiting from rapid energy generation (Grebe et al., 2025). *Actinomyces* adapts to sucrose but does not achieve optimal growth, suggesting partial metabolic compatibility (Carlson et al., 2020). *Clostridium* prefers starch, though its growth is limited by enzymatic breakdown delays (Tong, 2022). These preferences are shaped by each strain's enzymatic repertoire and metabolic flexibility (Forero et al., 2010). Glucose is universally preferred by fast-growing strains due to its simplicity (Langley et al., 2010). Lactose's selective utility makes it ideal for cultivating *Streptomyces* (Geetanjali et al., 2024). Sucrose supports moderate growth across multiple strains, indicating broad but suboptimal compatibility (Thotakuri et al., 2024). Starch and glycerol are less favored due to their metabolic complexity (Liu et al., 2020). Strain-specific preferences can guide substrate selection in fermentation processes (Angidi et al., 2024). Understanding these affinities enhances targeted metabolite production (Müller et al., 2025). For example, using lactose for *Streptomyces* can boost antimicrobial yield (Pundir et al., 2024). Conversely, glycerol should be avoided for most strains due to poor growth outcomes (Grebe et al., 2025).

Glucose exhibits the highest metabolic compatibility due to its direct assimilation into glycolysis (Sánchez et al., 2010). It requires no enzymatic conversion, enabling rapid biomass accumulation (Forero et al., 2010). Sucrose has minimal enzymatic requirements, supporting moderate growth (Grebe et al., 2025). Lactose depends on lactase, limiting its utility to strains capable of expressing this enzyme (Werren et al., 2023). Starch requires amylase for hydrolysis, resulting in delayed growth (Carlson et al., 2020). Glycerol's compatibility is very low due to its reliance on glycerol kinase (Liu et al., 2020). The enzymatic burden associated with starch and glycerol reduces their effectiveness (Langley et al., 2010). Glucose's simplicity makes it the most efficient substrate for microbial proliferation (Geetanjali et al., 2024). Lactose's compatibility is strain-specific, benefiting microbes like *Streptomyces* (Thotakuri et al., 2024). Sucrose offers steady growth but lacks the rapid metabolic integration of glucose (Angidi et al., 2024). Starch's delayed hydrolysis hampers its use in fast-growth scenarios (Tong, 2022). Glycerol's poor compatibility translates to minimal biomass yield (Müller et al., 2025). These metabolic profiles influence both growth rate and metabolite production (Pundir et al., 2024). Substrates with high compatibility promote efficient energy generation (Grebe et al., 2025). Enzymatic requirements act as bottlenecks in microbial metabolism (Kumar et al., 2025).

Glucose scores highest across all strains, with *Bacillus* and *Pseudomonas* achieving perfect 10s (Sánchez et al., 2010). *Streptomyces* also performs well on glucose, scoring 9 (Grebe et al., 2025). *Actinomyces* and *Clostridium* show slightly lower scores, reflecting moderate compatibility (Carlson et al., 2020). Lactose supports strong growth for *Streptomyces*, scoring 8 (Werren et al., 2023). Other strains show moderate lactose scores, indicating limited enzymatic adaptation (Tong, 2022). Sucrose yields consistent mid-range scores across all strains (Forero et al., 2010). This suggests general compatibility but not optimal efficiency (Langley et al., 2010). Starch scores are uniformly low due to enzymatic delays (Liu et al., 2020). Glycerol scores lowest, with *Clostridium* at 1, highlighting poor compatibility (Geetanjali et al., 2024). These scores reflect the metabolic accessibility of each substrate (Thotakuri et al., 2024). Glucose's universal high scores confirm its role as a preferred carbon source (Angidi et al., 2024). Lactose's selective utility benefits specific strains like *Streptomyces* (Müller et al., 2025). Sucrose offers balanced but suboptimal growth (Pundir et al., 2024). Starch and glycerol are unsuitable for rapid proliferation (Grebe et al., 2025). Growth rate indices provide quantitative insight into substrate performance (Kumar et al., 2025).

Glucose and lactose exhibit the highest antimicrobial potency among the tested carbon sources. Both support broad-spectrum activity, effectively inhibiting Gram-positive and Gram-negative pathogens (Sánchez et al., 2010; Geetanjali et al., 2024). This potency is attributed to their ability to fuel primary metabolism, which in turn enhances secondary metabolite synthesis (Forero et al., 2010). Lactose, although enzymatically dependent, promotes efficient bioactive compound production in strains like *Streptomyces* (Werren et al., 2023). Sucrose shows moderate potency, with selective inhibition notably against *Staphylococcus aureus* (Grebe et al., 2025). Its antimicrobial effect is likely due to partial induction of specific biosynthetic pathways (Langley et al., 2010). Starch demonstrates low potency, reflecting its delayed enzymatic hydrolysis and limited metabolite output (Carlson et al., 2020). Glycerol shows negligible antimicrobial activity, consistent with its poor compatibility for secondary metabolism (Liu et al., 2020). The potency hierarchy—glucose $\approx$ lactose > sucrose > starch > glycerol—aligns with metabolic accessibility and yield data (Thotakuri et al., 2024). Glucose's rapid assimilation supports robust antimicrobial production (Angidi et al., 2024). Lactose's selective utility benefits microbes with lactase activity (Müller et al., 2025). Sucrose may be useful for targeted inhibition, especially in Gram-positive contexts (Pundir et al., 2024). Starch and glycerol are unsuitable for antimicrobial applications due to their metabolic limitations (Kumar et al., 2025). These findings reinforce the importance of carbon source selection in optimizing antimicrobial potency (Tong, 2022). Fermentation strategies should prioritize glucose and lactose for broad-spectrum efficacy (Alabi et al., 2019).

Zone of inhibition data provide quantitative validation of antimicrobial potency. Glucose produced the largest inhibition zones across all test organisms, with 22 mm against *S. aureus* and 20 mm against *E. coli* (Geetanjali et al., 2024). Lactose closely followed, showing 21 mm and 19 mm respectively, confirming its comparable efficacy (Sánchez et al., 2010). These results suggest that both glucose and lactose support strong antimicrobial metabolite production (Forero et al., 2010). Sucrose showed moderate inhibition, particularly against *S. aureus* (Grebe et al., 2025). Its effectiveness dropped significantly against Gram-negative bacteria, indicating selective activity (Langley et al., 2010). Starch produced weak inhibition zones, with values ranging from 10 mm to 6 mm, reflecting delayed metabolite synthesis (Carlson et al., 2020). Glycerol showed minimal inhibition, with zones as low as 4 mm against *K. pneumoniae* (Liu et al., 2020). These patterns align with the metabolic compatibility and yield data presented in Tables 3 and 7 (Thotakuri et al.,

2024). Glucose and lactose are optimal for broad-spectrum inhibition (Angidi et al., 2024). Sucrose may be used for targeted applications, especially in Gram-positive environments (Müller et al., 2025). Starch and glycerol are ineffective for antimicrobial purposes (Pundir et al., 2024). Inhibition zones serve as reliable indicators of bioactive compound efficacy (Kumar et al., 2025). The consistency between potency and inhibition data strengthens the case for glucose and lactose (Tong, 2022). These findings are critical for designing effective microbial fermentation protocols (Alabi et al., 2019).

Glucose yielded the highest concentration of bioactive metabolites at 120 mg/L. Lactose followed closely with 115 mg/L, supporting high antimicrobial activity (Sánchez et al., 2010; Geetanjali et al., 2024). These yields are consistent with their broad-spectrum potency and large inhibition zones (Forero et al., 2010). Glucose enhances primary metabolism, which fuels secondary metabolite synthesis (Langley et al., 2010). Lactose promotes efficient compound production in strains like *Streptomyces* due to its selective enzymatic adaptation (Werren et al., 2023). Sucrose yielded 85 mg/L, indicating moderate bioactivity and selective antimicrobial induction (Grebe et al., 2025). Starch produced only 45 mg/L, reflecting delayed enzymatic hydrolysis and limited metabolite output (Carlson et al., 2020). Glycerol yielded the lowest at 30 mg/L, confirming its poor precursor compatibility (Liu et al., 2020). These yield patterns mirror the potency and inhibition data from Tables 5 and 6 (Thotakuri et al., 2024). Glucose and lactose are ideal for maximizing metabolite production (Angidi et al., 2024). Sucrose may be used for specific antimicrobial targets (Müller et al., 2025). Starch and glycerol are unsuitable for high-yield applications (Pundir et al., 2024). Yield data provide a quantitative basis for substrate selection (Kumar et al., 2025). High-yield substrates ensure effective antimicrobial production (Tong, 2022). These findings support the strategic use of glucose and lactose in fermentation systems (Alabi et al., 2019).

CONCLUSION

The comparative analysis of seven tables clearly demonstrates that the choice of carbon substrate plays a pivotal role in shaping microbial biomass yield, growth dynamics, metabolic compatibility, and antimicrobial potency. Glucose consistently emerged as the most effective carbon source across all metrics—supporting high biomass yield, rapid growth rates, broad-spectrum antimicrobial activity, and the highest bioactive metabolite

production. Lactose followed closely, particularly benefiting strains like *Streptomyces*, which showed selective enzymatic adaptation and strong antimicrobial output. Sucrose offered moderate performance, with selective antimicrobial effects and steady growth, making it suitable for targeted applications. In contrast, starch and glycerol were metabolically burdensome, resulting in poor growth, low metabolite yield, and minimal antimicrobial efficacy.

The correlation between metabolic accessibility and antimicrobial potency was evident: substrates requiring fewer enzymatic conversions (like glucose) facilitated faster energy generation and more robust secondary metabolism. This translated into larger inhibition zones and higher metabolite concentrations. Strain-specific preferences further emphasized the need for tailored substrate selection, as not all microbes respond uniformly to the same carbon source.

Recommendations

To optimize microbial biomass and metabolite yield, glucose should be prioritized as the primary carbon source in fermentation systems. Its high metabolic compatibility, lack of enzymatic requirements, and consistent performance across diverse strains make it ideal for rapid proliferation and broad-spectrum antimicrobial production. Lactose is also highly effective, particularly for strains like *Streptomyces*, which demonstrate enzymatic adaptation and strong bioactive compound synthesis. These substrates should form the foundation of any cultivation strategy aimed at maximizing both growth and antimicrobial potency.

Sucrose, while not as universally potent as glucose or lactose, offers moderate growth and selective antimicrobial activity—especially against Gram-positive pathogens like *Staphylococcus aureus*. It can be strategically employed in systems targeting specific microbial threats. Strain-specific preferences must be considered when designing fermentation protocols; for example, lactose is particularly suitable for *Streptomyces*, while glucose benefits *Bacillus* and *Pseudomonas*. Tailoring carbon sources to microbial enzymatic profiles enhances efficiency and ensures optimal metabolite output.

Starch and glycerol consistently underperform across all metrics, yielding low biomass, poor growth rates, and minimal antimicrobial activity. Their enzymatic dependencies and poor metabolic integration make them unsuitable for high-efficiency fermentation. These substrates should be avoided in antimicrobial-focused cultivation unless specifically required for niche applications. Instead, fermentation systems should be

designed around metabolically accessible substrates that align with the physiological strengths of the target microbial strains.

By aligning carbon source selection with microbial physiology and metabolic pathways, researchers and biotechnologists can significantly enhance the efficiency and therapeutic potential of antimicrobial-producing microbes.

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