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# Recycling Antibiotics into GUMBOS: A Novel Approach to Address Multi-Drug-Resistant Bacteria

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**Abstract**

Antimicrobial resistance (AMR) represents one of the most critical global health challenges, as multidrug-resistant (MDR) pathogens continue to rise, threatening the efficacy of conventional antibiotics. To combat this growing threat, innovative approaches, such as the recycling of antibiotics into Group of Uniform Materials Based on Organic Salts (GUMBOS), have emerged. GUMBOS are a novel class of compounds formed by combining antibiotics with counter-ions to modify their physicochemical properties, leading to enhanced antimicrobial activity, stability, and bioactivity. This review explores the design, mechanisms of action, and applications of GUMBOS, highlighting their potential in overcoming resistance, improving drug delivery, and offering new therapeutic options. The review also discusses the challenges and limitations, including toxicity concerns, scale-up difficulties, and regulatory hurdles. Furthermore, it emphasizes future perspectives, including the integration of GUMBOS with nanotechnology and their potential as a platform for broader drug repurposing. Although promising, the successful clinical translation of GUMBOS will require extensive in vivo studies and clinical trials to confirm their safety and efficacy. This approach not only


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presents a sustainable solution to AMR but also opens new avenues for the innovative delivery of therapeutic agents.

**Keywords:** GUMBOS, Multidrug-Resistant Bacteria, Antimicrobial Resistance, Drug Repurposing, Antibiotic Recycling, Nanotechnology, Drug Delivery

## Introduction

Antimicrobial resistance (AMR) has emerged as a critical global health threat, jeopardizing the effectiveness of existing antibiotics against a broad spectrum of bacterial pathogens. The World Health Organization (WHO) has projected that, without effective intervention, drug-resistant infections could lead to 10 million deaths annually by 2050, surpassing current mortality rates from cancer (World Health Organization, 2014). This alarming trend is primarily driven by the overuse and misuse of antibiotics in human medicine, agriculture, and animal husbandry, which collectively foster the development of multidrug-resistant (MDR) bacteria (Ventola, 2015).

The proliferation of MDR bacteria significantly impairs the efficacy of current therapeutic options, rendering common infections increasingly difficult to treat. This escalation leads to prolonged illnesses, elevated mortality rates, and substantial economic burdens on healthcare systems worldwide (O'Neill, 2014). In response to this pressing issue, there is an urgent need for innovative strategies to combat AMR.

One promising approach involves the repurposing of existing antibiotics through chemical modifications to enhance their activity against resistant strains. A novel concept in this domain is the development of Group of Uniform Materials Based on Organic Salts (GUMBOS).(Costa et al., 2023). GUMBOS are ionic liquids composed of organic cations and anions, engineered to possess specific physicochemical properties, including reduced volatility, high thermal stability, and the ability to solvate a wide range of active pharmaceutical ingredients (Azevedo et al., 2020). These characteristics make GUMBOS particularly suitable for drug delivery applications, offering potential solutions to overcome the limitations associated with conventional antibiotic formulations.

Integrating antibiotics into GUMBOS presents a multifaceted strategy to address AMR. By encapsulating antibiotics within GUMBOS, it is possible to achieve controlled release, enhanced solubility, and improved bioavailability, thereby maximizing therapeutic

outcomes while minimizing side effects. Moreover, the tunable nature of GUMBOS allows for the design of formulations that can effectively interact with bacterial membranes, potentially restoring the efficacy of antibiotics against resistant strains (Cole et al., 2015).

Incorporating GUMBOS into antibiotic therapy aligns with the principles of green chemistry, aiming to develop sustainable and environmentally friendly pharmaceutical interventions. The versatility of GUMBOS extends beyond drug delivery; they can also serve as solvents for the extraction of bioactive compounds, permeation enhancers in transdermal applications, and as platforms for the development of stimuli-responsive drug delivery systems (Jordan & Gathergood 2013).This review aims to explore the potential of recycling antibiotics into GUMBOS as a novel approach to combat multidrug-resistant bacteria. By examining the current advancements in GUMBOS-based drug delivery systems, their mechanisms of action, design strategies, and comparative studies with conventional antibiotics, we seek to provide a comprehensive understanding of their role in addressing the challenges posed by AMR. Furthermore, the review will address the applications, challenges, and future perspectives of GUMBOS in the context of antibiotic resistance, highlighting their promise as a transformative tool in modern pharmaceutical science.

## Discussion

### *Understanding GUMBOS: A Novel Approach to Antibiotic Enhancement*

### *What are GUMBOS?*

Group of Uniform Materials Based on Organic Salts (GUMBOS) are ionic compounds formed by pairing organic cations with various anions, resulting in materials with unique and tunable physicochemical properties. These properties include solubility, melting point, thermal stability, and bioactivity, which can be adjusted by selecting appropriate cation-anion combinations. This tunability makes GUMBOS particularly suitable for applications in drug delivery and antimicrobial therapy (Cole, Hobden, & Warner, 2015).

### How Do GUMBOS Differ from Traditional Ionic Liquids?

While both GUMBOS and traditional ionic liquids are composed of ionic species, they differ significantly in their physical states and applications. Traditional ionic liquids are typically liquid at room temperature and are often used as solvents or catalysts in chemical

reactions. In contrast, GUMBOS are designed to be solid at ambient temperatures, offering advantages in stability and ease of handling. Their solid-state allows for easier incorporation into various formulations, such as topical creams or oral dosage forms, enhancing their practicality in pharmaceutical applications (Cole et al., 2015).

The customizable nature of GUMBOS provides several significant advantages:

(1) Customizable Structure: The cation and anion components of GUMBOS can be varied to optimize desired properties, such as solubility and bioactivity, tailoring them for specific therapeutic applications (Cole et al., 2015).
(2) Enhanced Bioactivity: By pairing antibiotics with specific counter-ions, GUMBOS can exhibit improved antimicrobial properties, including enhanced efficacy against resistant bacterial strains (Costa et al., 2023). And
(3) Reduced Volatility: The solid-state nature of GUMBOS minimizes volatility concerns, leading to improved stability and shelf-life compared to their liquid counterparts (Cole et al., 2015).

**The Concept of Recycling Antibiotics**

In the context of GUMBOS, "recycling" refers to the process of repurposing existing or outdated antibiotics by converting them into GUMBOS, thereby restoring or enhancing their antimicrobial efficacy. This approach offers a novel pathway to combat antibiotic resistance by revitalizing compounds that may have lost effectiveness due to resistance mechanisms.

**Repurposing Old or Ineffective Antibiotics into GUMBOS**

The conversion of traditional antibiotics into GUMBOS involves pairing them with specific counter-ions to form ionic salts. This transformation can lead to improved solubility, stability, and, in some cases, enhanced antimicrobial activity. For example, pairing β-lactam antibiotics with chlorhexidine diacetate has resulted in GUMBOS with potent activity against multidrug-resistant bacteria, offering a promising strategy to overcome existing resistance (Cole et al., 2015).

**Potential to Overcome Resistance Through Physicochemical Property Changes**

The alteration of physicochemical properties during the formation of GUMBOS can impact the interaction between antibiotics and bacterial cells. Changes in solubility, membrane permeability, and the ability to evade bacterial efflux pumps can contribute to

overcoming resistance mechanisms. By modifying these properties, GUMBOS may restore the effectiveness of antibiotics against resistant strains, providing a valuable tool in the fight against antimicrobial resistance (Costa et al., 2023).

## Mechanism of Action and Antimicrobial Activity of GUMBOS

### Interaction with Bacterial Membranes

GUMBOS (Group of Uniform Materials Based on Organic Salts) exhibit enhanced antimicrobial properties through their interaction with bacterial membranes. The pairing of antibiotics with counter-ions in GUMBOS can lead to increased membrane permeability, facilitating the entry of the antimicrobial agent into the bacterial cell. This mechanism is particularly effective against multidrug-resistant (MDR) strains, as demonstrated by studies involving β-lactam-based chlorhexidine GUMBOS, which showed improved activity against both Gram-positive and Gram-negative bacteria, including MDR strains like Methicillin-resistant *Staphylococcus aureus* (MRSA) and Carbapenem-resistant *Enterobacteriaceae* (CRE) (Cole, Hobden, & Warner, 2015).

### Enhanced Permeability and Sustained Release

The structural characteristics of GUMBOS contribute to their ability to enhance bacterial membrane permeability and provide sustained release of the antibiotic. By modifying the physicochemical properties of antibiotics through GUMBOS formation, it is possible to achieve prolonged antimicrobial effects, reducing the frequency of dosing and potentially improving patient compliance. For instance, studies have shown that GUMBOS formed from fluoroquinolones exhibited good performance against Gram-negative *Escherichia coli*, indicating potential for sustained-release formulations. (Muteeb et al., 2023).

### Studies Against MDR Strains

Research has demonstrated the efficacy of GUMBOS against various MDR bacterial strains. In vitro studies have shown that GUMBOS formed from β-lactam antibiotics and chlorhexidine diacetate inhibited the growth of MDR strains at lower concentrations compared to unreacted mixtures of the precursor ions. For example, GUMBOS required approximately 25 to 3,400 times fewer moles than β-lactam antibiotics to inhibit MRSA strains, highlighting their potential in combating resistant infections (Azevedo et al., 2024).

## Design Strategies for GUMBOS

### Choosing the Right Antibiotic and Counter-Ion

The selection of appropriate antibiotics and counter-ions is crucial in designing effective GUMBOS. The antibiotic should have intrinsic activity against the target bacteria, while the counter-ion should enhance the antimicrobial properties without introducing toxicity. Studies have demonstrated that pairing chlorhexidine diacetate with β-lactam antibiotics resulted in GUMBOS with superior activity against Gram-positive bacteria, including MRSA, compared to unreacted mixtures (Cole et al., 2015).

### Tuning Hydrophobicity, Solubility, and Charge

Adjusting the hydrophobicity, solubility, and charge of GUMBOS is essential to optimize their antimicrobial efficacy and pharmacokinetic properties. These parameters influence the ability of GUMBOS to interact with bacterial membranes, penetrate cells, and release the active antibiotic. For instance, studies involving ciprofloxacin-based GUMBOS have shown that modifications can lead to enhanced antibacterial performance against Gram-negative *Klebsiella pneumoniae*

### Examples from Literature

Ciprofloxacin-GUMBOS: Research has demonstrated that ciprofloxacin-based GUMBOS exhibit enhanced antibacterial activity against Gram-negative bacteria. The incorporation of ciprofloxacin into GUMBOS has shown improved performance against *Klebsiella pneumoniae* compared to free ciprofloxacin, highlighting the potential of GUMBOS in enhancing the efficacy of existing antibiotics (Costa et al., 2023).

Tetracycline-GUMBOS: Studies have explored the formation of GUMBOS using tetracycline and various counter-ions. These GUMBOS have demonstrated promising antimicrobial activity, offering potential alternatives to conventional tetracycline formulations, especially against resistant bacterial strains.

### Comparative Studies: GUMBOS vs. Conventional Antibiotics

Group of Uniform Materials Based on Organic Salts (GUMBOS) have emerged as a promising strategy to enhance the efficacy of conventional antibiotics, particularly against

multidrug-resistant (MDR) bacterial strains. Comparative studies evaluating GUMBOS alongside traditional antibiotics have provided valuable insights into their potential advantages.

Minimum Inhibitory Concentration (MIC) Values, Biofilm Penetration, and Resistance Development Rate

Research indicates that GUMBOS often exhibit superior antibacterial activity, requiring lower concentrations to inhibit bacterial growth compared to their conventional counterparts. For instance, studies involving β-lactam-based chlorhexidine GUMBOS demonstrated enhanced activity against Gram-positive bacteria, including methicillin-resistant *Staphylococcus aureus* (MRSA). These GUMBOS inhibited MRSA strains at concentrations approximately 25 to 3,400 times lower than the unreacted antibiotic mixtures, highlighting their potential in combating resistant infections (Cole, Hobden, & Warner, 2015).

Regarding biofilm penetration, GUMBOS have shown promise in disrupting biofilms formed by MDR bacteria. The enhanced permeability and sustained release properties of GUMBOS facilitate deeper penetration into biofilm matrices, potentially leading to more effective eradication of biofilm-associated infections (Cole et al., 2015).

While specific studies on the resistance development rate of GUMBOS are limited, their unique mechanisms of action suggest a reduced likelihood of resistance development. The synergistic effects between antibiotics and counter-ions in GUMBOS may delay or prevent the emergence of resistance, although further research is necessary to confirm this hypothesis.

**Stability and Shelf-Life Improvements**

The solid-state nature of GUMBOS contributes to their enhanced stability and extended shelf-life compared to traditional liquid antibiotics. Studies have shown that GUMBOS formed from β-lactam antibiotics and chlorhexidine diacetate exhibit favorable physical properties, including reduced solubility and improved dissolution rates, which are associated with increased stability (Cole et al., 2015). Additionally, the reduced volatility of GUMBOS minimizes degradation due to evaporation, further contributing to their prolonged shelf-life.

comparative studies suggest that GUMBOS offer several advantages over conventional antibiotics, including lower MIC values, enhanced biofilm penetration, potential reduction in resistance development, and improved stability and shelf-life. These attributes position GUMBOS as a promising alternative in the ongoing battle against antibiotic-resistant bacterial infections.

Additionally, recent work by Bakare-Abidola et al. (2025) demonstrated the sustainability and reusability of [C12MIm] [DS]-based GUMBOS embedded in alginate beads, achieving a maximum methylene blue (MB) adsorption capacity of 4.5 mg/g and maintaining 57.6% removal efficiency after six adsorption-desorption cycles. This highlights their broader potential as eco-friendly and reusable materials not only for environmental remediation but also for biomedical applications such as drug delivery systems.

## Applications and Delivery Approaches of GUMBOS

### *Potential for Topical, Systemic, or Surface Coatings*

Group of Uniform Materials Based on Organic Salts (GUMBOS) have emerged as versatile candidates for various biomedical applications, including topical treatments, systemic administration, and surface coatings. Their unique physicochemical properties, such as tunable hydrophobicity and bioactivity, make them suitable for these diverse applications.

### *Topical Applications*

Topical administration of GUMBOS offers several advantages, particularly in wound healing and infection control. Their ability to form stable, bioactive films can provide a protective barrier against pathogens while promoting tissue regeneration. For instance, GUMBOS have been incorporated into wound dressings, enhancing antimicrobial activity and supporting the healing process. Studies have demonstrated that incorporating antimicrobial agents into wound dressings can effectively reduce infection rates and accelerate healing.

### *Systemic Applications*

The systemic use of GUMBOS is facilitated by their customizable solubility and stability profiles. By modifying the counter-ions, the pharmacokinetic properties of the parent drugs can be optimized, leading to improved bioavailability and therapeutic efficacy. This approach is particularly beneficial for drugs with poor solubility or stability issues. Research

indicates that GUMBOS can enhance the delivery and effectiveness of various therapeutic agents.

### *Surface Coatings*

Applying GUMBOS as surface coatings on medical devices can impart antimicrobial properties, reducing the risk of device-related infections. The incorporation of GUMBOS onto surfaces can prevent bacterial adhesion and biofilm formation, which are critical factors in the development of infections associated with medical implants. Studies have shown that surface modifications with antimicrobial agents can significantly decrease microbial colonization on medical devices.

## Biomedical Devices and Wound Dressings

GUMBOS have significant potential in the development of advanced biomedical devices and wound dressings. Their ability to incorporate antimicrobial agents, growth factors, or other bioactive molecules makes them ideal candidates for enhancing wound healing. For example, GUMBOS can be integrated into hydrogel-based dressings, providing a moist healing environment while delivering therapeutic agents directly to the wound site. This strategy aligns with current trends in wound care, where dressings not only protect but also actively contribute to the healing process.

## Challenges and Limitations

Despite their promising applications, several challenges must be addressed before GUMBOS can be widely adopted in clinical settings.

### *Toxicity and Biocompatibility Concerns*

Ensuring the safety of GUMBOS is paramount. While the modification of drug properties can enhance efficacy, it is crucial to assess the potential cytotoxicity and overall biocompatibility of these compounds. Comprehensive in vitro and in vivo studies are necessary to evaluate any adverse effects. Research in this area is ongoing, aiming to balance the antimicrobial benefits of GUMBOS with their safety profiles.

### *Scale-Up and Synthesis Costs*

The transition from laboratory-scale synthesis to commercial production of GUMBOS presents logistical and economic challenges. Scalability issues, such as maintaining

consistent quality and yield, need to be addressed. Additionally, the cost of synthesizing GUMBOS must be evaluated to ensure that they are economically viable for widespread use. Studies have highlighted the need for cost-effective production methods to facilitate the translation of GUMBOS from research to practical applications.

***Regulatory Hurdles***

Introducing GUMBOS into the market requires navigating complex regulatory pathways. Regulatory agencies require extensive data on the safety, efficacy, and manufacturing processes of new biomedical materials. The unique nature of GUMBOS may necessitate the development of new guidelines and standards. Collaboration between researchers, industry, and regulatory bodies is essential to streamline the approval process.

GUMBOS represent a promising advancement in biomedical materials, offering diverse applications ranging from topical treatments and systemic drug delivery to surface coatings for medical devices. Their integration into wound care products aligns with the trend towards multifunctional, bioactive dressings that actively contribute to healing. However, addressing challenges related to toxicity, production scalability, and regulatory approval is essential for the successful translation of GUMBOS from the laboratory to clinical practice. Continued research and development are crucial to fully harness the potential of GUMBOS in medical applications.

## Future Perspectives

### Integration with Nanotechnology and Smart Delivery Systems

The integration of GUMBOS (Group of Uniform Materials Based on Organic Salts) with nanotechnology holds significant promise for advancing drug delivery systems. By combining the tunable properties of GUMBOS with nanoscale engineering, researchers can develop smart delivery systems capable of precise targeting and controlled release of therapeutic agents. For instance, nanoGUMBOS have demonstrated selective toxicity towards cancer cells, sparing normal cells, and have been effective in isolating hemoglobin from human blood, indicating their versatility in biomedical applications .

### GUMBOS as a Platform for Broader Drug Repurposing

Beyond their application in combating multidrug-resistant bacteria, GUMBOS offer a novel platform for drug repurposing. By pairing existing drugs with various counter-ions, it

is possible to enhance their efficacy, modify their pharmacokinetic properties, and overcome current limitations. This approach allows for the rejuvenation of older drugs with diminished effectiveness, potentially extending their clinical utility and providing new therapeutic options.

## Need for In Vivo Studies and Clinical Trials

While in vitro studies have elucidated the potential of GUMBOS and nanoGUMBOS, there is a critical need for in vivo studies and clinical trials to fully assess their safety, efficacy, and therapeutic potential. Animal studies are essential to evaluate the pharmacokinetics, biodistribution, and long-term effects of these compounds. Subsequent clinical trials will be necessary to confirm their suitability for human use, determine appropriate dosing regimens, and identify any potential adverse effects.

## Conclusion

GUMBOS represent a significant advancement in the field of drug delivery, offering customizable properties that can be tailored for specific therapeutic applications. Their integration with nanotechnology paves the way for developing smart delivery systems capable of targeted and controlled release, enhancing drug efficacy while minimizing side effects. The potential of GUMBOS extends to the repurposing of existing drugs, providing new avenues for treatment options. However, to translate these promising findings into clinical reality, extensive in vivo studies and clinical trials are imperative. Addressing these research needs will determine the role of GUMBOS in the future of medicine, potentially revolutionizing drug delivery and therapeutic strategies.

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