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Innovation in Advanced Bioactive Biomaterials for 3D Printing

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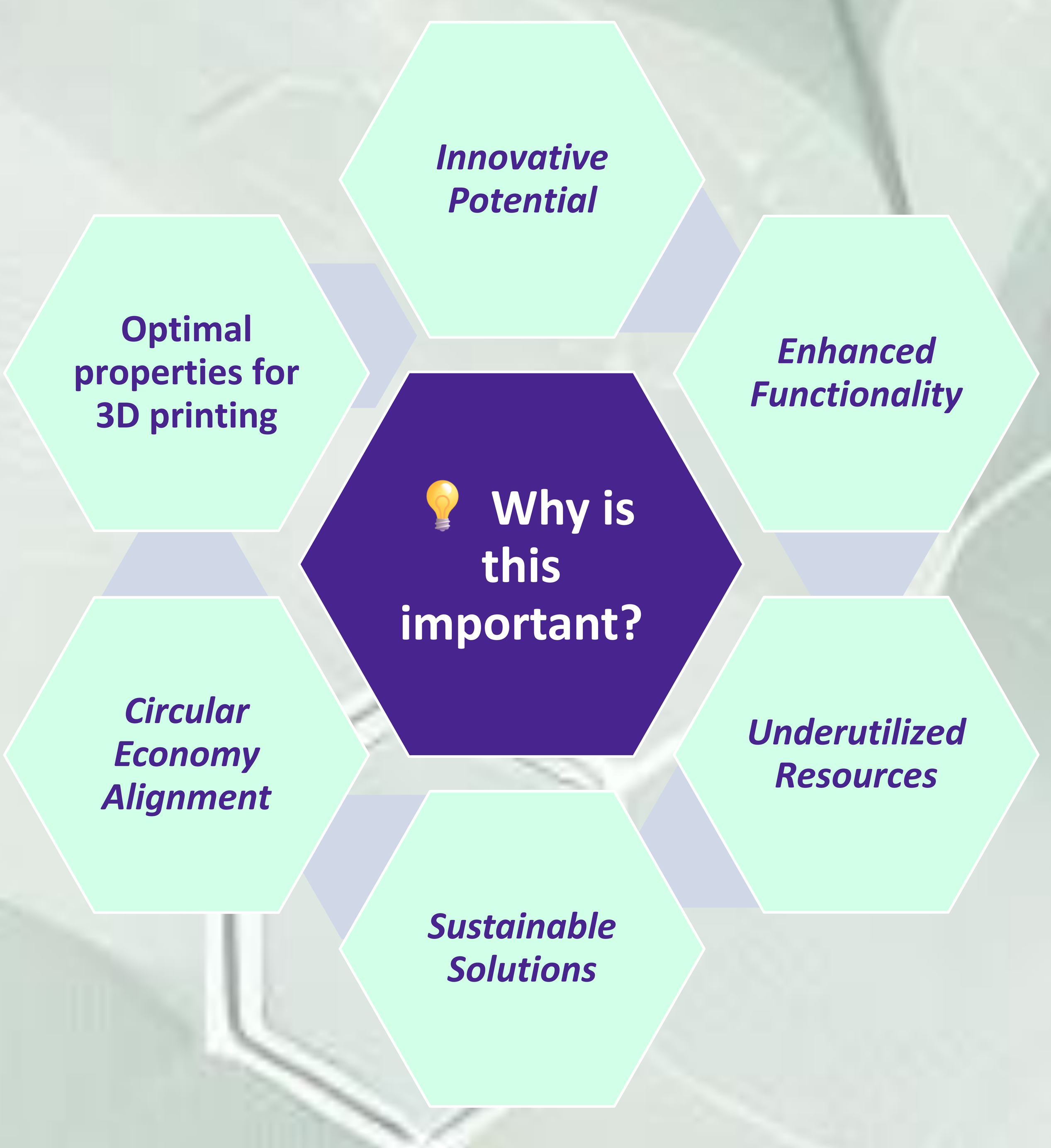
Abstract

- Recent advances in **3D printing technologies** have significantly expanded the possibilities in **biomedical engineering**, especially through the development of advanced **bioactive biomaterials**.
- This review explores the latest **innovations** in the **design**, **synthesis**, and **application** of bioactive materials tailored for 3D printing, with a focus on their role in **tissue engineering**, **regenerative medicine**, and **personalized healthcare solutions**.
- We examine categories such as **bioceramics**, **natural and synthetic polymers**, **composite hydrogels**, and **bioinks** enhanced with **nanoparticles** or **biologically active agents**.
- Key criteria such as **biocompatibility**, **printability**, **mechanical stability**, and **biodegradability** are discussed in relation to their suitability for **additive manufacturing processes**.
- The integration of **smart functionalities** - such as **antimicrobial activity**, **controlled drug release**, or **cell signaling modulation** - is highlighted as a **transformative trend** in the development of **next-generation biomaterials**.



Methodology

PRISMA 2020 (Preferred Reporting Items for Systematic Reviews and Meta-Analyses)

The methodology was structured to ensure transparency and reproducibility in the identification, selection, and synthesis of relevant literature concerning bioactive biomaterials for 3D printing in biomedical applications.

Literature Search Strategy
- multiple databases: **PubMed**, **Scopus**, **Web of Science**, and **Google Scholar**
- covering the period **January 2015 to December 2024**
- the search terms: combinations of keywords such as *"bioactive biomaterials," "3D bioprinting," "bioceramics," "bioinks," "hydrogels," "tissue engineering,"* and *"regenerative medicine"*
- boolean operators (AND, OR) were used to refine search results and increase specificity.

Inclusion Criteria
- Peer-reviewed articles published in English
- Focus on the synthesis, characterization, or application of bioactive materials in 3D printing
- Relevance to biomedical fields, particularly tissue engineering and regenerative medicine
- Discussion of key properties such as **biocompatibility**, **printability**, **mechanical stability**, **biodegradability**, and **smart functionalities**

Exclusion Criteria
- Non-biomedical applications
- Non-peer-reviewed articles, editorials, or conference abstracts
- Duplicates or studies lacking methodological clarity

Study Selection and Data Extraction
- **two independent reviewers** who screened the titles and abstracts for relevance; disagreements were resolved through discussion or consultation with a third reviewer

Critical Appraisal and Synthesis
- focused on performance metrics (e.g., mechanical properties, degradation rate), bioactivity, and potential for clinical translation

Results & Discussion

Potential of Agro-Industrial By-Products in Bioactive Biomaterials
- **Rich Source of Bioactive Compounds**
- **Sustainability and Circular Economy**
- **Enhanced Functional Properties**

Integration into Polymeric Matrices for 3D Printing
- **Synergy of Natural and Synthetic Polymers**
- **Improved Biocompatibility**
- **Structural Integrity in 3D Printing**

Advantages of Bioactive 3D-Printed Biomaterials
- **Biocompatibility**
- **Bioactivity**
- **Controlled Degradation**
- **Mechanical Stability**

Topic	Key Findings	Discussion	Examples
Material Performance	Bioactive materials show ***improved printability and mechanical properties***	Enhanced rheological properties contribute to ***structural fidelity and functional performance*** post-printing	Composite hydrogels with nanocellulose or graphene oxide improve both **stiffness and cell adhesion**
Biological Response	***High biocompatibility and cell viability*** observed across multiple studies	Supports ***tissue integration*** and promotes ***cell proliferation and differentiation***	GelMA and alginate blends support **stem cell growth and osteogenic differentiation**
Functional Integration	***Smart functionalities*** successfully incorporated in experimental models	Antimicrobial and drug-releasing properties increase ***therapeutic potential***	Bioinks with silver nanoparticles or encapsulated antibiotics prevent **infection post-implantation**
Challenges in Translation	***Material scalability*** and ***regulatory approval*** remain significant hurdles	Lab success does not guarantee ***clinical or commercial adoption*** without long-term validation	Compliance testing and GMP manufacturing limitations slow down **market entry**
Research Gaps	Limited data on long-term in vivo performance and degradation profiles	Further ***in vivo and clinical studies*** are needed to ensure material safety and functionality	Lack of longitudinal studies with large animal models or human trials
Future Opportunities	Combining bioprinting with ***AI and machine learning*** for material design and optimization	Potential to accelerate discovery of ***tailor-made bioinks*** for personalized medicine	Use of AI to predict material behavior and **optimize scaffold architecture** automatically

Conclusions

The results of this study highlight the potential of **underexploited agro-industrial bioresources** for obtaining **valuable bioactive compounds** with applications in skin regeneration biomaterials.

The developed polymeric compositions exhibit **optimal properties for 3D printing** and favorable interactions with skin cells, supporting the **advancement of new therapeutic strategies**.

Future studies will focus on **evaluating the performance** of these biomaterials in **advanced experimental models**.

Acknowledgements

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