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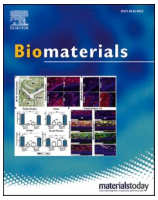

The emerging role of bile acids as critical components in nanotechnology and bioengineering: Pharmacology, formulation optimizers and hydrogel-biomaterial applications

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ABSTRACT

The role of endogenous bile acids as lipid stabilizers aiding uptake of lipophilic nutrients via micelle formation and saponification effects is well documented and precedes their growing applications in pharmaceutical sciences. Their utility stems from their unique physico-chemical profile and ability to modulate immune cell signalling pathways. It has been shown that bile acids alter specific receptor-mediated pathways of cellular respiration and metabolism, providing potential clinical therapies for cardio-metabolic disorders such as diabetes mellitus, hypercholesterolemia, and heart disease. Additionally, some bile acids exert profound anti-oxidant, anti-inflammatory and immunosuppressant properties, and are effective at reducing blood pressure and alleviating hypertension.

Their unique amphoteric properties and proven ability as permeability enhancers make them a desirable pharmaceutical excipient. When incorporated with various carbohydrates, polymers, hydrogels and/or polyelectrolytes to form micro- or nano-capsules, they provide enhanced thermodynamic, osmotic and structural stability, and cater for controlled delivery via specific tissue targeting, pH dependant release and temperature guided sol-gel complexation. Additionally, due to their immunosuppressant properties, they enhance the immunogenicity of encapsulated cells, increasing the feasibility of bioartificial organs as transplantable therapeutics.

This review explores existing and future applications of bile acids and provides a synopsis of their role in advanced, novel therapeutic delivery systems.

1. Introduction

Many diseases and traumas can cause irreparable damage to the tissue through acute or chronic insults, resulting in a complete or partial lack of function. For example, the autoimmune component of Type 1 diabetes is responsible for destruction to insulin-secreting beta cells, rendering endocrine parts of the pancreas non-functional, while acute ischemic insults in any tissue decrease its functionality and limit survival. So far, while there are instances of successful mitigation of complete or partial tissue dysfunction (thyroid hormone replacement therapy in case of removed thyroid gland), the majority of organ failures and terminal stages of progressive chronic diseases require deteriorated tissue to be replaced or repaired, usually through organ transplantation. An alternative to surgery is the utilization of injectable cell delivery

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Table 2
Studies using BA in cell delivery systems.

Bile acid	Polymer	Tissue	Form	Reference
UDCA	Alginate	Islets/β-cells	Microcapsules	[1,42,93,94,124,254]
CA	Alginate	B-cells	Microcapsules	[255]
TCA	Alginate	B-cells	Microcapsules	[256]

5. Conclusion

This review outlines the emerging role of BAs in the homeostasis of endocrine, gastrointestinal, immune, and cardio-metabolic biological systems, and how their unique pharmacological and physico-chemical properties contribute to potential roles in the new areas of biomaterials research, with a key focus on the creation of artificial organs. The ability of endogenous BAs to modify key cellular signalling pathways attributed to graft rejection, fibrosis, and tissue necrosis, could dramatically alter the science of transplantation and xenograft research, and perhaps re-examine the widespread use of immunosuppressants in clinical practice. Future research is needed to best guide the clinical manifestations of BA-mediated artificial organs, and to determine the benefits of BAs as pharmacological agents in the management of immune related disorders.

Data availability

All data is available upon request to the corresponding author.

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Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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