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Digest paper

# Non-enzyme entrapping biohydrogels in catalysis

Marleen Häring [a,1], Markus Tautz [a,1], Juan V. Alegre-Requena [b,1], César Saldías [c], David Díaz Díaz [a,d,*]

[a] Institut für Organische Chemie, Universität Regensburg, Universitätsstr. 31, 93053 Regensburg, Germany
[b] Department of Chemistry, Colorado State University, Fort Collins, USA
[c] Departamento de Química Física, Facultad de Química, Pontificia Universidad Católica de Chile, Casilla 302, Correo 22, Santiago, Chile
[d] IQAC-CSIC, Jordi Girona 18-26, 08034 Barcelona, Spain

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ABSTRACT

This review provides an overview of the current status and future directions of the use of biohydrogels (i.e., hydrogels obtained from biopolymers) as heterogeneous catalysts and/or supports for catalytic metal nanoparticles. This review collects a wide variety of biohydrogels used in catalytic applications, including gels made of polysaccharides (chitosan, alginate, carrageenan, dextran, agarose), proteins (gelatin, silk fibroin, ferritin) and nucleic acids (DNA). Additionally, the most significant features about the recyclability of these materials, their structural properties and the type of reactions that they catalyze are discussed.



**Contents**



## Introduction

The concern about deterioration of the environment is constantly growing in modern society as demonstrated by stringent governmental regulations. The lack of clear information on the safety of some chemicals established on some markets as well as on the amount of hazardous substances being released into the environment during the use and disposal of chemical products in many countries will continue driving a major challenge to policy makers over the next years. Within this context, during the last few decades chemists have made remarkable progresses to replace petrochemical-based products with environmentally friendly and

* Corresponding author at: Institut für Organische Chemie, Universität Regensburg, Universitätsstr. 31, 93053 Regensburg, Germany.
*E-mail address:* David.Diaz@chemie.uni-regensburg.de (D. Díaz Díaz).
[1] Equal contribution.

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sustainable resources [1,2]. In this sense, many biopolymers have shown unique properties (e.g., unlimited availability as renewable agro-resources, non-toxicity, biodegradability, insolubility in most organic solvents, high binding ability for selected metals) [3] that make them promising environmentally benign supports for heterogeneous catalysis [4,5]. In addition, the successful development of biopolymer-based catalysts that are biocompatible, robust and can be mass-produced can be very important for designing "greener catalysts" in the future (See Table 1).

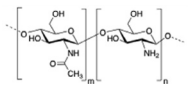
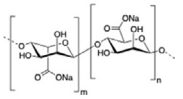
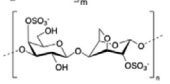
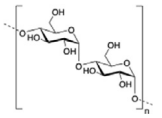
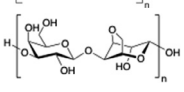
Among different properties of the biopolymers, their ability to form hydrogels (refereed here as biohydrogels) at low concentrations has been extensively used for biomedical, health care, food and cosmetic applications [6]. Moreover, their high mechanical strength, stimuli-responsive behavior, good diffusion properties and the presence of reactive functionalities on the polymer backbone have also stimulated their application in the field of catalysis. Similarly, physical (supramolecular) gels made of low-molecular-weight (LMW) compounds have also gained popularity as potential reaction vessels and/or nanoreactors and have been summarized in a previous review [7].

In this review, we have gathered the most relevant results appeared during the last decade regarding biohydrogels with promising properties as heterogeneous recyclable catalysts. Even though the introduction of these gels to real-life applications is still in a preliminary stage, we strongly believe that this review could show the potential that these materials have for some catalytic processes. Materials such as dried gels (aerogels) [3,8], biopolymer-based non-hydrogel systems used in catalysis –even when they were used in aqueous medium– (i.e., hyaluronic acid [9], keratin [10], pullulan [11], cellulose [12], glucomannan [13], pectin [14], starch [15], collagen [16]), and enzyme-containing hydrogels [17] have been extensively described elsewhere and are out of the scope of this contribution. Finally, a comparison of the performance of the biohydrogels with some other methods reported in the literature for the same chemical transformations is given in the Annex.

## Chitosan-based hydrogels

In a seminal work by Paradossi and co-workers [18], a $Cu^{2+}$-loaded chitosan-based hydrogel ($Cu^{2+}$-CSH) was prepared using a polyfunctionalized β-cyclodextrin as cross-linking agent.

**Table 1**
Molecular structures of biopolymers used in the preparation of catalytic hydrogels described in this review. Proteins such as gelatin, silk fibroin, ferritin and DNA are not shown.

| Biopolymer | Structure |
|---|---|
| Chitosan |  |
| Sodium alginate |  |
| κ-carrageenan |  |
| Dextran |  |
| Agarose |  |

This metallohydrogel was found to be an efficient, heterogeneous and recyclable catalyst for the oxidation of adrenaline (**1**) to **2** by molecular oxygen in aqueous media (Fig. 1).

Kinetic studies carried out at different substrate concentrations showed the oxygen depletion in the dispersion during the catalytic oxidation of adrenaline (Fig. 1, plot). The results indicated a first-order mechanism with respect to $O_2$. No significant differences were observed in the slope of the kinetic runs between L-adrenaline and its racemic mixture, indicating the absence of stereoselective control due to the chirality of the saccharidic moiety.

In 2012, we reported the first comprehensive study aimed to establish the intrinsic catalytic properties of unmodified chitosan hydrogel beads (CSHB) as a green organocatalyst for C—C bond forming reactions [19]. Uniform-size spherical hydrogel beads (average diameter = 4.0 ± 0.1 mm) were prepared by alkaline coagulation of an acidic viscous chitosan solution added using a dropping funnel (Fig. 2A–C).

One of the most crucial aspects during the evaluation of the CSHB catalyst is the meticulous washing protocol of the matured beads until neutral pH, thereby ensuring the removal of trapped hydroxyl ions, which otherwise might influence the base catalysis by the free amino groups —$NH_2$ on the chitosan [20]. Scanning electron microscopy (SEM) images of the corresponding freeze-dried CSHB showed the heterogeneous porous network nature of the beads with pores up to 2 mm in diameter (Fig. 2D and E), in contrast to the amorphous structure of commercially powdered chitosan (Fig. 2F). Such morphological features can strongly favor the adsorption of small molecules and ions presented in the medium via electrostatic interactions (non-specific or physical adsorption), hydrogen bonding and/or van der Waals forces [21]. The aqueous swelling of the CSHB was translated in a much higher percentage of accessible —$NH_2$ groups (55–65%) in comparison to both powdered commercially chitosan (PCS) and dried chitosan beads (2.5 and 1.7%, respectively), which was expected to enhance the potential base catalytic activity of the former.

Regardless the molecular weight of the chitosan, CSHB (pH ≈ 6.6–6.9) showed in general very low activity towards direct aldol reactions between aldehydes and ketones. However, different reac-

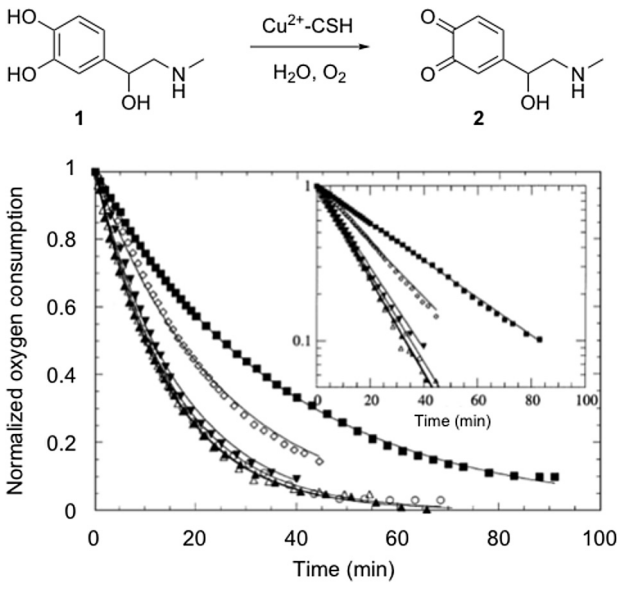



**Fig. 1.** Kinetics of the oxygen consumption in the reaction of oxidation of adrenaline promoted by a chitosan-based hydrogel developed by Paradossi's group. L-adrenaline concentration: (○) 1.47 mM; (Δ) 1.37 mM; (▲) 0.95 mM; (◇) 0.50 mM; (■) 0.17 mM. (±) adrenaline concentration: (▼) 1.37 mM. Adapted with permission from Ref. [18]. Copyright 1997, Elsevier B.V.