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Sulphotransferases: Enabling green and effective sulphation of bioactive complex molecules

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PURPOSE OF THE ABSTRACT
The sulphation of biomolecules is a widespread process in nature, which occurs in various organisms, ranging from prokaryotes to multicellular species, and numerous biological functions are associated with this crucial transformation.1 The enzymes responsible for sulphation are sulphotransferases, which transfer the sulphate group from the 3′-phosphoadenosine-5′-phosphosulfate (PAPs) cofactor to the substrate of interest.2 Among the different molecules which could be sulphated, steroids represent an intriguing class since these compounds play a significant role in several pathophysiological processes.3 Given the increasing interest in these molecules and the limitation of conventional chemical sulphation—that involves the use of toxic reactants, harsh conditions, and results in mediocre selectivity—4 alternative biocatalytic methods are highly desirable. That being said, enzymatic sulphation has been poorly investigated to date: the high cost and instability of the PAPs required cofactor make the biocatalytic approach indeed extremely challenging. To address this issue and expand the previously limited substrate scope, inspired by nature we developed a biocatalytic sulphation approach that employs an enzymatic cascade for in-situ synthesis and regeneration of the cofactor from cheap and readily available ATP and p-nitrophenol. Furthermore, novel sulphotransferases that are active on steroids have been identified through a survey of the biochemistry literature as well as an analysis of protein and genome databases. These enzymes have been recombinantly expressed in E. coli in good yields and obtained in highly purified form. In conclusion, this biocatalytic strategy along with a new toolbox of sulphotransferases would allow the sulphation not only of steroids but also of many structurally diverse molecules.

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FIGURES

FIGURE 1

FIGURE 2

KEYWORDS

sulphation | enzymatic cascade | steroid | cofactor regeneration

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