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Functionalized materials for multistage platforms in the oral delivery of biopharmaceuticals

Francisca Araújo [a,b,c,d], José das Neves [a,b], João Pedro Martins [d], Pedro L. Granja [a,b,c], Hélder A. Santos [d,e], Bruno Sarmento [a,b,f,*]

[a] i3S – Instituto de Investigação e Inovação em Saúde, Universidade do Porto, 4200-135 Porto, Portugal
[b] INEB – Instituto de Engenharia Biomédica, Universidade do Porto, 4200-135 Porto, Portugal
[c] ICBAS – Instituto Ciências Biomédicas Abel Salazar, Universidade do Porto, 4150-180 Porto, Portugal
[d] Division of Pharmaceutical Chemistry and Technology, Faculty of Pharmacy, University of Helsinki, FI-00014 Helsinki, Finland
[e] Helsinki Institute of Life Science, HiLIFE, University of Helsinki, FI-00014 Helsinki, Finland
[f] CESPU, Instituto de Investigação e Formação Avançada em Ciências e Tecnologias da Saúde, 4585-116 Gandra, Portugal

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ABSTRACT

Recent developments in materials science and specific surface functionalization of materials are providing new tools for the rational design of precisely engineered drug delivery systems. Particular interest has been paid to the exploitation of functionalized materials in the administration of biopharmaceuticals by the oral route, traditionally challenging and frequently compromised when using conventional pharmaceutical approaches. Using such materials for producing particulate systems is a common approach to obtain advanced drug delivery systems capable of providing stable and biocompatible environments and allowing for a targeted delivery of the associated biopharmaceuticals. This work intends to provide a thorough, up-to-date and holistic discussion on specific engineering and surface functionalization strategies of multistage platforms towards the development of novel delivery platforms for oral drug administration, with particular focus on the different materials and their interactions at the biological-material-host interface. This review will also address the safety and toxicity concerns of the resulting drug delivery systems, as well as their regulatory status and pathway towards the market approval of novel biopharmaceutical products based on particulate delivery systems.

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* Corresponding author at: i3S – Instituto de Investigação e Inovação em Saúde da Universidade do Porto, Portugal and INEB – Instituto de Engenharia Biomédica, Universidade do Porto, Rua Alfredo Allen, 208, 4200-135 Porto, Portugal.
E-mail address: bruno.sarmento@ineb.up.pt (B. Sarmento).

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1. Introduction

More than ever, the field of materials science is providing interesting tools to meet the challenge of developing drug carriers that are able to orally deliver biopharmaceuticals in a controlled manner, and overcome the gastrointestinal hurdles in order to enhance their bioavailability [1]. Although a once rarely used subset of the medical armamentarium, biomolecules have evolved over recent decades as very promising entities in therapeutics, prophylaxis and diagnostics of disease, introducing the concept of biotherapy (Fig. 1) [2].

The materials used for biopharmaceuticals delivery, and thereof drug carriers, are somehow engineered to have some characteristics, such as biocompatibility and biodegradability, which makes them biomaterials. The field of biomaterials has around 50 years of history and covers many fundamental areas, such as biology, chemistry, materials science and tissue engineering [3]. However, since biomaterials intimately interact with biological systems, their use is not straightforward and some considerations must be taken into account when developing drug delivery systems, such as the choice of the most suitable material to be used and the delivery route. It must be stressed that the establishment of a material–tissue interface will lead to mutual direct and counter responses. Also, after exposure to a biological environment, biomaterials will undergo several and sequential changings that may modify their original properties [4].

Biomaterials in the form of particulate carrier systems have been shown to be able to protect and transport various biopharmaceuticals until the intestine, such as insulin, glucagon like peptide-1 (GLP-1) and vitamin B12 upon oral delivery,

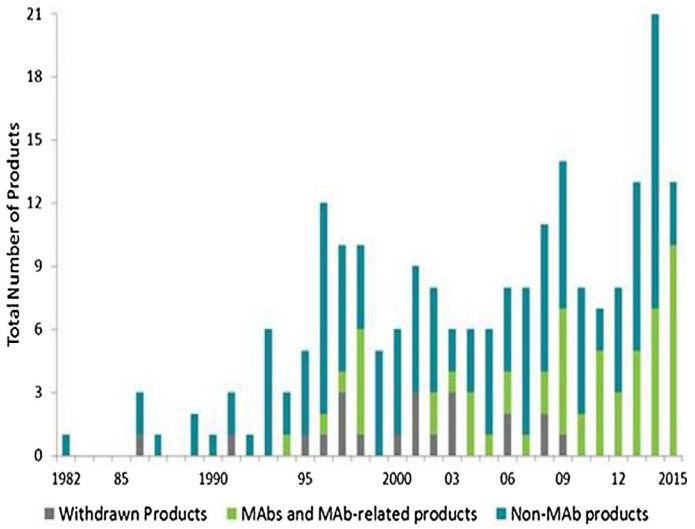

Fig. 1. Biopharmaceuticals annual approvals 1982–2015. The figure displays de number of products first approved for commercial sale in the US or Europe each year since 1982. Products approved but subsequently removed from the market are denoted in grey; MAb and Mab-related products are shown in green; non-Mab-related products are shown in blue. For 2015, the figure includes the number of products approved as of December 31 [313].