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Review

Hyperbranched polyglycerols at the biointerface

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ABSTRACT

The control over biointerfacial interactions is the key to a broad range of biomedical applications, ranging from implantable devices to drug delivery and nanomedicine. In many of these applications, coatings are required that reduce or prevent non-specific interactions with the biological environment, while at the same time presenting specific bioactive signals. Whilst surface coatings based on polymers such as poly(ethylene glycol) (PEG) have been used successfully, many limitations persist in regard to the biocompatibility, stability and functionality of state-of-the-art polymer coatings. Most of these limitations are related to the fact that, typically, linear polymers are used with associated limited chemical functionality. Here, we examine the development of hyperbranched polyglycerols (HPGs) as promising candidates for the replacement of traditional linear polymers, such as the chemically analogous PEG, for the control of biointerfacial interactions. HPGs are highly branched globular molecules that exhibit a high valency, allow easy access to a variety of functionalities and can present biologically active signals. In this review, a comprehensive overview is provided with respect to the history, synthetic strategies, modifications and applications of HPGs.

Contents

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1. Introduction

Increasingly sophisticated applications in fields such as biotechnology, nanotechnology and medicine have pushed traditional linear polymers to their limits. This has set a trend in polymer science leading away from basic linear structures towards increasingly complex polymeric architectures [1]. With the aim of creating macromolecules that could fulfil multiple prerequisites, dendrimers have become popular because of their precise, well-defined structures and high levels of functionality. The globular structure and high valency exhibited by dendrimers provide many benefits unobtainable by linear polymers. Dendrimers are defined by their symmetric molecular structure resulting from defined branching at every addressable functional group. This is followed by deprotection or activation to generate new addressable groups, which undergo branching in a subsequent step. The stepwise synthesis creates a layered structure, with each layer referred to as a generation. In theory, each dendrimer generation has an exact molecular weight and a polydispersity of 1. However, the arduous and time-consuming stepwise synthesis and typically low yields are a significant drawback for dendrimers when it comes to practical applications [2]. Hyperbranched polymers in comparison combine aspects of both linear and dendritic polymers. Randomly throughout the polymer, a chain can either propagate as a linear section, or it can branch as a dendritic section. The ratio of dendritic and linear sections of a hyperbranched polymer, also referred to as the degree of branching (DB), can determine characteristics of the polymer such as conformation, density and viscosity. As the DB approaches 1, the characteristics of hyperbranched polymers become closer to those observed for dendrimers [3].

Therefore, hyperbranched polymers can be viewed analogues to dendrimers in regard to their functionality, structure and conformation. However, they differ significantly in their synthesis and purification [1,4]. While hyperbranched polymer structures are not as well defined as dendrimers, they share similar multivalent and globular macrostructures, and can therefore be used in many applications as a suitable substitute. Importantly, hyperbranched polymers can be synthesised in a single step reaction with high yields. Not surprisingly, hyperbranched polymers are becoming increasingly popular as a cheap and relatively simple to produce alternatives to dendrimers.

Hyperbranched polymers as a whole have been described before in several outstanding reviews, [1,2,4–6]. Therefore, we have focussed specifically on one system: hyperbranched polyglycerols (HPGs). In this review, we are covering the most important techniques for HPG synthesis, modifications that are important for practical applications, properties and here in particular biocompatibility and conclude with a discussion on future prospects for this polymer system. While a broad overview of HPGs is given here, we have focussed on issues related to biomedical applications, such as biocompatibility and the use of HPGs for the control of biointerfacial interactions. Only a limited number of studies have used HPGs tethered to a solid substrate, but HPG-based coatings have emerged as promising candidates for applications such as antifouling coatings and drug delivery vehicles. HPGs provide significant advantages, for example in regard to stability and functionality, over current benchmark coatings based on PEGs. It is therefore expected that HPGs will be effective tools for a broad range of biomedical applications *in vitro* and *in vivo*. Our review only covers work involving hyperbranched polyglycerols as opposed to previous reviews by Haag et al. and Frey et al. which specifically cover dendritic polyglycerols [7,8].