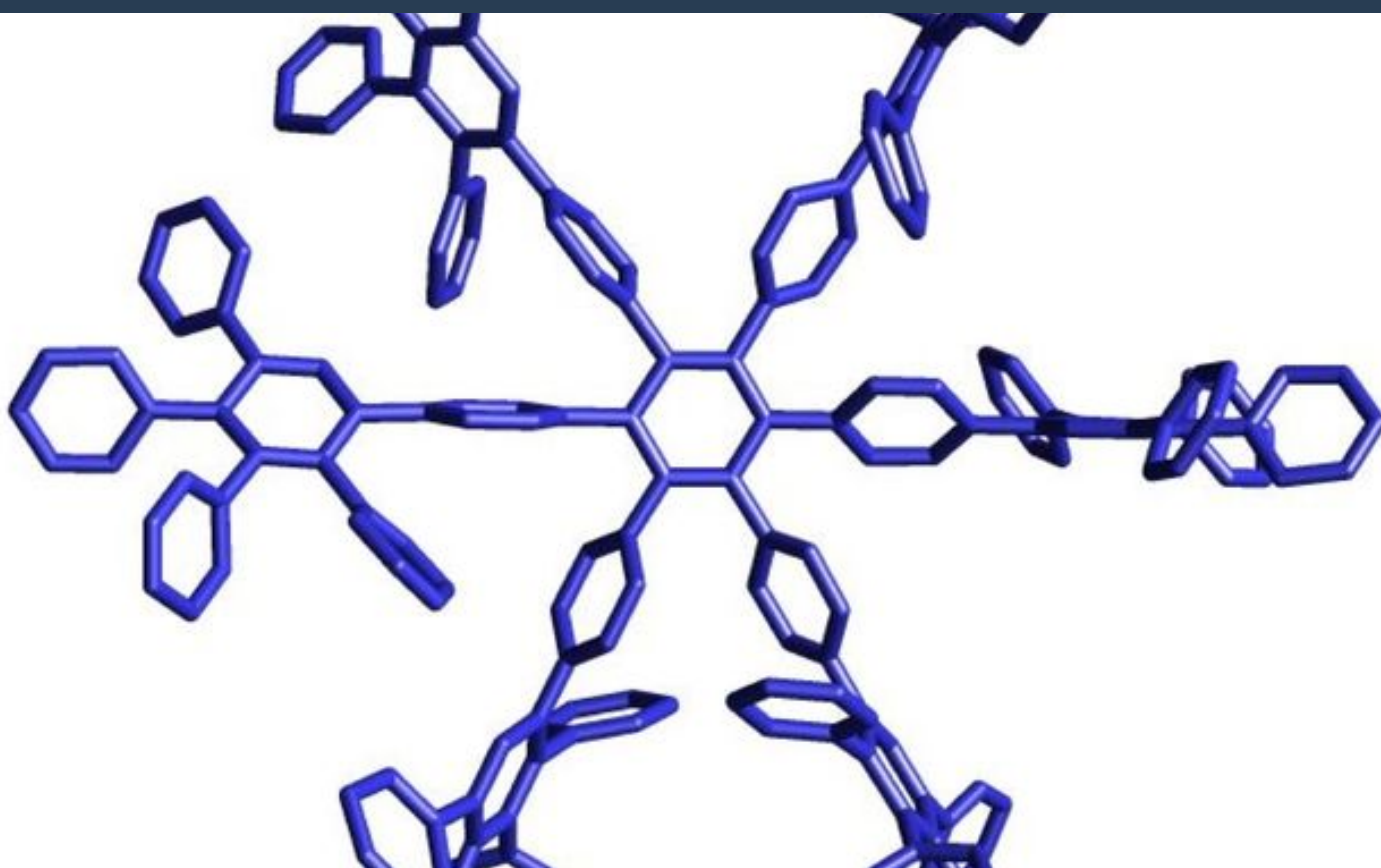


Hyperbranched Polydendrons - A Unique Dendrimer Analogue Platform Technology

A chemistry strategy for HPD synthesis that utilises low generation dendron-based initiators and chain-growth branching polymerisation



Please note, header image is purely illustrative. Source: M Stone, en.Wikipedia.org, CC BY-SA 3.0.

IP Status

Patented

Seeking

Development partner, Commercial partner

About **University of Liverpool**

By facilitating access to our expertise, facilities and networks, the University of Liverpool offers the means to transform ideas into creative solutions, improved performance, new technologies, strategies, applications, products or skills.

Background

Dendrimers are a novel materials class with the major benefits of a) globular structures, b) distinct exterior and interior locations, c) multi-functional surfaces, d) encapsulation/release. Despite their unique properties, the range of dendrimer applications remains relatively limited due to a number of limitations, not least of which are the constraints around their synthesis. These include: 1) the complex iterative synthetic procedures, 2) the use of organic chemistry reactions (e.g. condensation) to generate the internal structure (and ultimately the mass and multiplicity) of the dendrimer, 3) the lack of flexibility to control/vary the core chemistry (most dendrimer cores utilise a single repeating AB_n monomer), 4) the difficulty in reaching high molecular weights, 5) the considerable chemical losses at each iterative step (including analytical, work up, purification and reaction solvent waste), and 6) the relative difficulty in mixing functionality.

Recent patented materials synthesis routes (grants in several countries) developed by the University of Liverpool has addressed many of these limitations by merging the speed of polymer chemistry with the ideal branching of dendrimer chemistry. The new materials, named *hyperbranched*-Polydendrons (HPDs) offer many synthetic benefits, new opportunities not available to dendrimer chemists, ability to readily tune behaviour, and the potential for the formation of highly uniform structures with environmental response.

Tech Overview

The chemistry strategy for HPD synthesis (**Figure 1**) utilises low generation dendron-based initiators (to minimise cost and synthetic complexity) and chain-growth branching polymerisation to tie together the resulting linear-dendritic hybrid structures in a single-step one-pot reaction. The polymers that are formed are highly functional, fully soluble, un-crosslinked architectures as governed by having less than one branching group per primary chain.

Stage of Development

The HPD platform has been utilised in a predominantly academic setting however ongoing studies are employing HPDs to encapsulate anti-cancer drugs. Nanoprecipitation (**Figure 2**) has been extremely successful and very low dispersity nanoparticles with varying nanoparticle sizes (60-800 nm). Through incorporation of PEG mixed initiator systems, the ratio of PEG/dendron may be controlled, allowing the simple introduction of steric stabilisation to the resulting nanoparticles (**Figure 3**) which also tailors the interaction with biological systems. This approach has also been able to generate patchy particles with reactive chemistries that may be modified post-polymerisation, allowing the HPD to act as a scaffold that can be modified with a range of chemistries after its synthesis. Mucoadhesive properties of these and related materials has also been established.

Benefits

The synthesis of HPDs offers a range of benefits that are not available through conventional dendrimer chemistry (Figure 4). This comes predominantly from the chemical flexibility of utilising chain-growth polymerisation to rapidly generate the core of the structure. Variation can be utilised through a) monomer structure/chemistry: the core of the HPD can be generated, in principle, from any vinyl double bond therefore the hydrophilicity, hydrophobicity, glass transition temperature, encapsulation and rigidity may be tuned to specific applications; b) primary chain length: the internal length of the primary chain building blocks may be varied to manipulate the weight % of the final material that is generated from the surface dendrons and the overall molecular weight of the HPD – molecular weights of >106 g/mol have been achieved, bearing >300 functional groups; c) dendron type and generation: flexibility is easily introduced to control the number of dendron functional groups, mixed functionality and mixed dendron chemistry within the same sample; d) through mixed-initiation, combinations with non-dendritic initiators are readily generated (e.g. addition of PEG chains); e) brancher chemistry: cleavable branchers have been introduced to induce degradation of the complex architectures back to low molecular weight fragments, and f) primary chain chemistry: the use of controlled radical polymerisation and ROP have been demonstrated – ROP to form branched polyester (e.g. caprolactone) HPDs has been accomplished. This level of flexibility is not available through the iterative reaction of AB_n monomers in conventional dendrimer synthesis.

Opportunity

A number of peer-reviewed articles have been published to date and the team at UoL are actively following ongoing programmes to extend the scope of the platform. In addition, the novel nature of the materials has led to a portfolio of related patents which cover a range of HPD, modified HPD and branched polymer surfactants (including mucoadhesive emulsions and nanoemulsions). These patents are all owned by the University of Liverpool and are listed below.

The university seek to develop interaction with appropriate companies to discuss potential opportunities to utilise dendrimers; allowing access to the HPD platform and the opportunity to develop cheaper and more flexible platforms to address defined applications commercially.

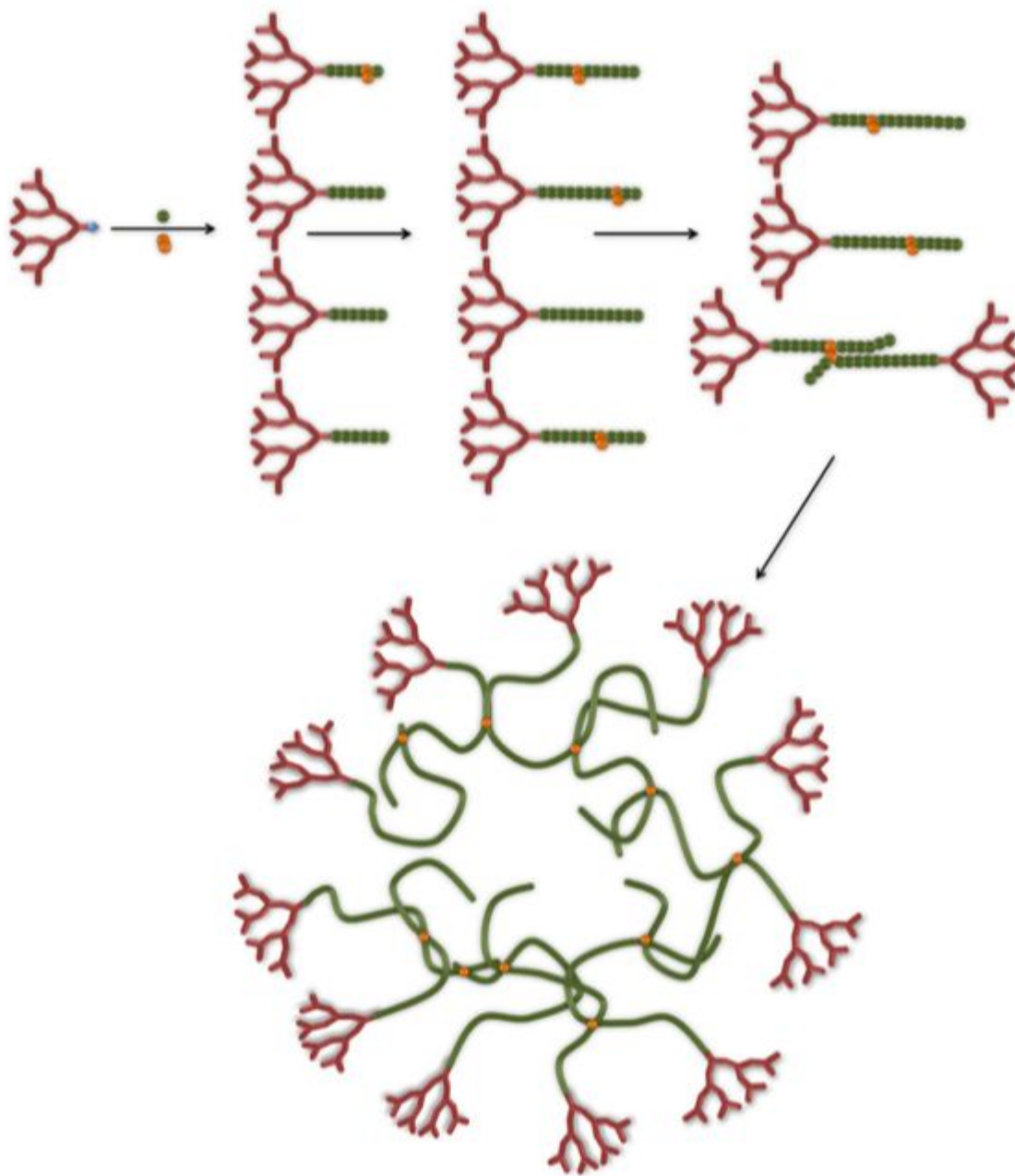
Patents

- WO 2009/122220 – Hyperbranched Polydendron (current grant status – USA (plus divisional); EU (plus divisional, China, Canada, India);
- WO 2014/199174 – Mixed initiators for HPDs;
- WO 2014/199175 – pH responsive HPDs;
- WO 2016/124925 – Nanoemulsions for oral drug delivery;
- WO 2016/009227 – Branched and linear block copolymer co-nanoprecipitation;
- WO 2017/118842 – HPDs from polyester ROP;
- PCT/GB2017/052334 – Mucoadhesive emulsions.

Appendix 1

Figure 1

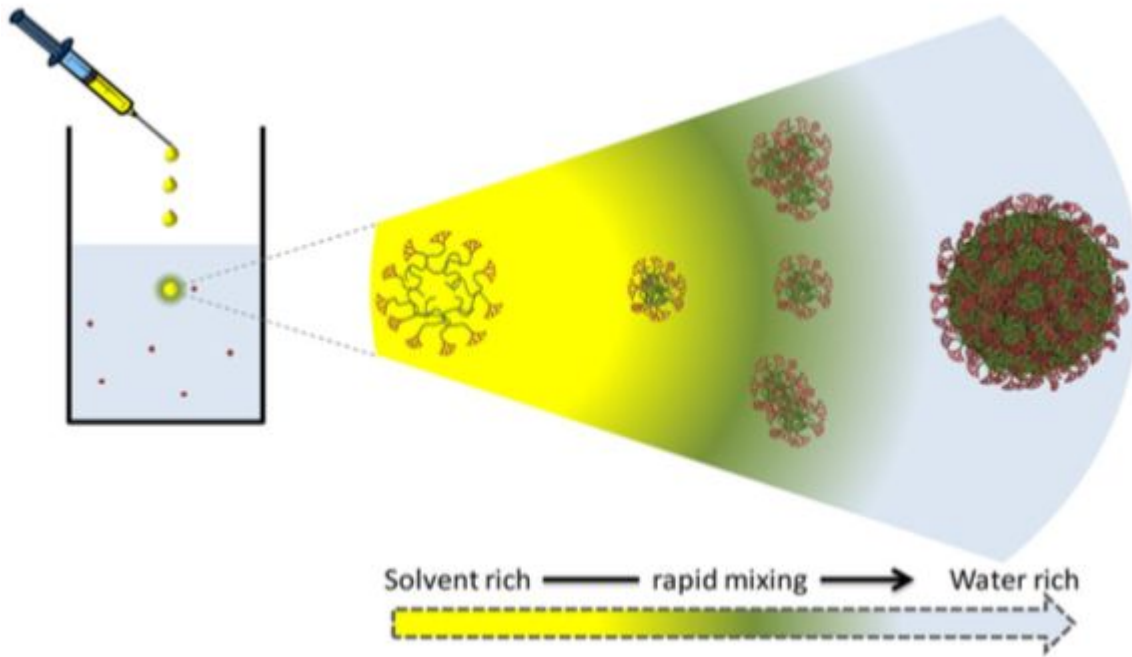
Schematic representation of the hyperbranched - Polydendron synthesis strategy.



Appendix 2

Figure 2

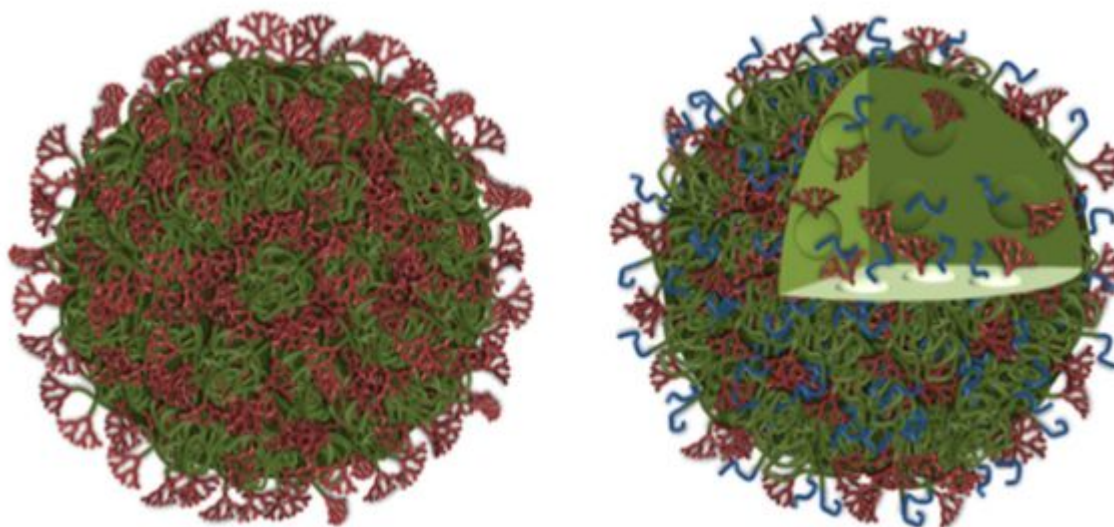
Nanoprecipitation of hyperbranched - Polydendrons.



Appendix 3

Figure 3

Schematic representation of HPDs with varying dendron/PEG.



Appendix 4

Figure 4

Structural variation available through hyperbranched - Polydendrons.

