



Technology Summary: Polyethylene Glycol Omega-amino Acid

Opportunity Statement

Polyethylene glycol (PEG) has several chemical properties that make it especially useful in various biological, chemical and pharmaceutical settings including the following:

- Non-toxic and non-immunogenic – Can be added to media and attached to surfaces and conjugated to molecules without interference with cellular functions or target immunogenicities.
- Hydrophilic (aqueous-soluble) – Attachment to proteins and other biomolecules decreases aggregation and increases solubility.
- Highly flexible – Provides for surface treatment or bioconjugation with less steric hindrance.

PEGylation is the process of covalent attachment of PEG polymer chains to another molecule - normally a drug or most typically peptides, proteins, and antibody fragments - that can help to meet the challenges of improving the safety and efficiency of many therapeutics. PEGylation is routinely achieved by incubation of a reactive derivative of PEG with the target macromolecule. It produces alterations in the physiochemical properties including changes in conformation, electrostatic binding and hydrophobicity. These physical and chemical changes increase the systemic retention of the therapeutic agent. It can also influence the binding affinity of the therapeutic moiety to the cell receptors and can alter the absorption and distribution patterns.

The covalent attachment of PEG to a drug or therapeutic protein can "mask" the agent from the host's immune system, thereby reducing immunogenicity and antigenicity. It also increases the hydrodynamic size of the agent, which prolongs its circulatory time by reducing renal clearance. PEGylation can also provide water solubility to hydrophobic drugs and proteins, increase drug stability, reduce dosage frequency and enhance protection from proteolytic degradation.

Problem

Despite the growing use of functionalized PEG in drugs on the market and in the development pipelines, there is still a substantial room for improvement in parameters such as solubility, complexity, purity and functionalization.

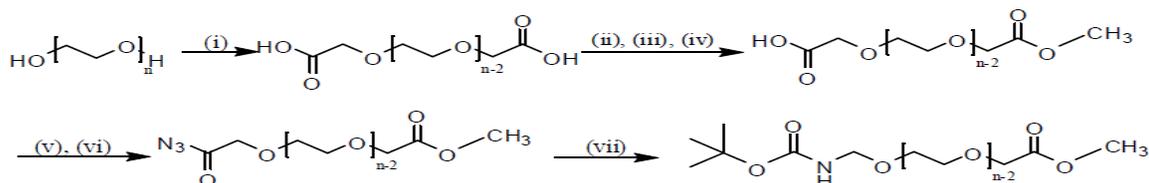
Therefore, there is a need for the development of a PEG-based solution that substantially improves upon the benefits of competing approaches.

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360ip Partner's Solution

360ip partner's invention is a novel PEG omega-amino acid structure that allows the PEG to have two ends, one amine termini and one carboxyl termini protected. The amine termini can be activated and conjugated to other chemicals under acidic conditions. The carboxyl termini can be activated and conjugated to other chemicals under alkaline conditions. This enables selective conjugation of the termini to the chemical of interest. This property also has the additional benefit of preventing the amine terminal from reacting with the carboxyl terminal.

The invention also involves a preparation method for synthesizing PEG omega-amino acid that involves a solid-phase reaction, azidation reaction and Curtius rearrangement reaction. This overcomes the complicated separation and purification in the synthesis of PEG omega-amino acid of the existing methods.



(i) TEMPO/NaBr/NaClO; (ii) 2-Chlorotriethyl chloride resin/DIEA; (iii) CH₃OH/DCC/DMAP; (iv) TFA/DCM(1%);
(v) Et₃N, ClCOOC₂H₅; (vi) NaN₃/H₂O; (vii) (CH₃)₃COH

The partner's technology has the following advantages:

- Moderate reaction conditions
- Short synthetic route (reaction time 35-40 hours)
- Simple separation and purification (column chromatography)
- Yield of more than 70%
- Purity of ~ 95%
- Materials used are less toxic as compared to epoxy ethane used in conventional PEG compounds.

Patents

360ip's partner has filed one patent application on this technology and plans to seek protection in multiple jurisdictions.

360ip is seeking interested parties for the licensing, further development and commercialization of this technology-based product.

For additional information, contact:

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