PEGYLATION

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1 PEGYLATION

1.1 History

The pioneering first steps in PEGylation were taken in late 1970 in the laboratory of Frank Davis of Rutgers University [1]. In late 1970s, PEGylation was first reported by Davies and Abuchowski in two key research papers on albumin and catalase modification [2, 3]. This was an important milestone because at that time it was not conceivable to modify an enzyme while maintaining its activity. Since then, the research on the PEGylation process expanded and developed tremendously [4]. The covalent attachment of polyethylene glycol (PEG) to enzymes, proteins, peptides, and nonpeptides, a process known as PEGylation, has received increased attention [5] nowadays.

Abuchowski et al., [2] altered the immunological properties of bovine serum albumin (BSA), which was achieved by the covalent attachment of PEG. With this achievement, the exploration of PEG chemistry started [6].

1.2 Definition

Different researchers have defined PEGylation in their own words. PEGylation involves the masking of the surface of proteins and peptides by covalent coupling with soluble PEG [1]. It is a method for optimizing pharmacokinetic and pharmacodynamic properties of therapeutic small drug molecules such as peptides and proteins [7].

Thus, it can be concluded that PEGylation is the modification of the surface properties of proteins and peptide or nonpeptide molecules via covalent attachment using a chemical modifier, PEG, either alone or in combination with other moieties. PEGylation has been exploited to increase the half life ($t_{1/2}$), solubility, stability and decrease of the immunogenicity, and toxicity of enzymes, proteins, peptides, and nonpeptide molecules.

1.3 PEGnology

PEGnology, as the name indicates, is the study of the modifications of proteins, peptides, or nonpeptides by associating them with PEG [8]. Frank F. Davis, of Rutgers University, New Jersey, is known as "father of PEGnology." While browsing in medical journals, he came across an article that explained how physicians infused a solution containing a mild surfactant, a block copolymer of PEG and polypropylene glycol into the blood of patients undergoing major vessel surgery in order to prevent the formation of lipid embolisms [8]. This was when he focused on PEG [8] and started his work with methoxy PEG.

2 PEGYLATION OF THERAPEUTIC AGENTS

2.1 Proteins and Peptides

Many differences exist among proteins/peptides and conformational low-molecular-weight (MW) compounds,

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