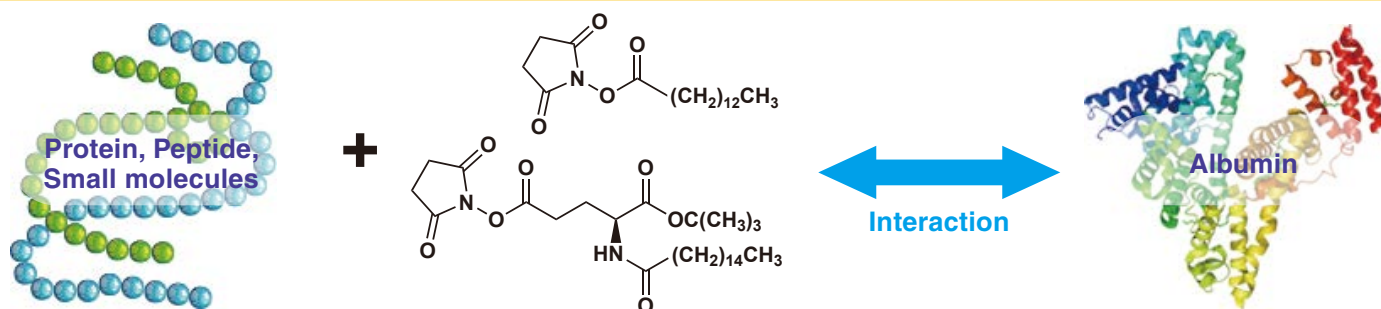


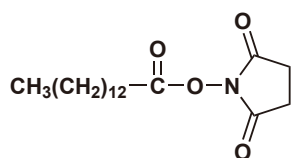
Human-Serum-Albumin Binding Agents for Improvement of Pharmacokinetics

Useful for Drug Kinetics Studies



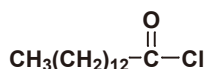
In pharmaceuticals, pharmacokinetics is one of the important factors for drug efficacy. Pharmacokinetics of drugs and contrast agents is optimized by introducing fatty acids and some small molecules which have affinity with human serum albumin. Recently, several insulin drugs having a regulated half-life in blood by modification with fatty acids such as myristic acid or palmitic acid have been developed and approved. Fatty acid derivatives reported to bind with albumin are shown below. Diphenylcyclohexane derivatives are also presented. These reagents are available as building blocks for optimization of pharmacokinetics with peptides generally having a short half-life in blood.

Myristoylation Reagents



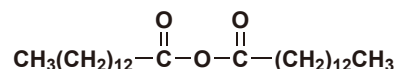
Myristic Acid *N*-Succinimidyl Ester

1g / 5g
[S0997]



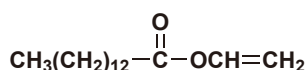
Myristoyl Chloride

25g / 400g
[T0086]



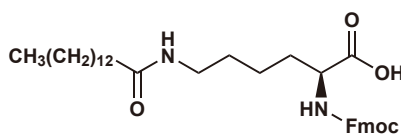
Myristic Anhydride

25g / 250g
[M0484]



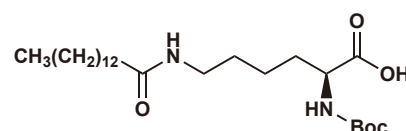
Vinyl Myristate

25mL / 500mL
[M0723]



N^α-Fmoc-*N*^ε-tetradecanoyl-L-lysine

1g / 5g
[F1143]



N^α-Boc-*N*^ε-tetradecanoyl-L-lysine

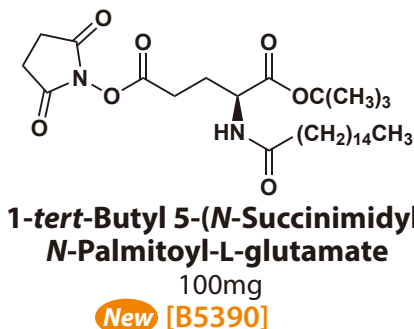
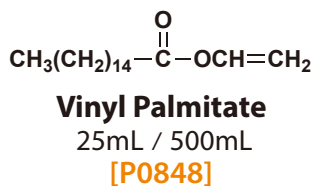
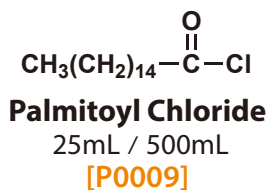
200mg / 1g
[B5366]

Applications

- 1) Albumin binding of insulins acylated with fatty acids: characterization of the ligand-protein interaction and correlation between binding affinity and timing of the insulin effect *in vivo*
P. Kurtzhals *et al.*, *Biochem. J.* **1995**, 312, 725.
- 2) Insulin Mimetic Action of Synthetic Phosphorylated Peptide Inhibitors of Glycogen Synthase Kinase-3
B. Plotkin *et al.*, *J. Pharmacol. Exp. Ther.* **2003**, 305, 974.
- 3) Design of the Novel Protraction Mechanism of Insulin Degludec, an Ultra-long-Acting Basal Insulin
I. Jonassen *et al.*, *Pharm. Res.* **2012**, 29, 2104.
- 4) Myristic acid-modified thymopentin for enhanced plasma stability and immune-modulating activity
W. Su *et al.*, *Int. Immunopharmacol.* **2017**, 47, 88.

Human-Serum-Albumin Binding Agents for Improvement of Pharmacokinetics

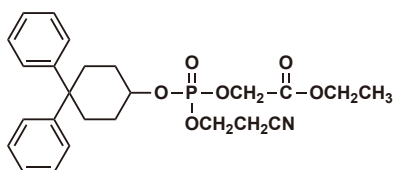
Palmitoylation Reagents



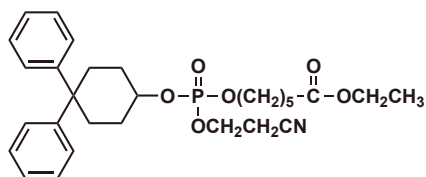
Applications

- 1) Acylation of human insulin with palmitic acid extends the time action of human insulin in diabetic dogs
S. Myers *et al.*, *Diabetes* **1997**, 46, 637.
- 2) Potent Derivatives of Glucagon-like Peptide-1 with Pharmacokinetic Properties Suitable for Once Daily Administration
L. B. Knudsen *et al.*, *J. Med. Chem.* **2000**, 43, 1664.
- 3) Lipidation of Cysteine or Cysteine-Containing Peptides Using the Thiol-Ene Reaction (CLipPA)
M. A. Brimble *et al.*, *Eur. J. Org. Chem.* **2016**, 2608.

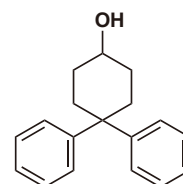
Diphenylcyclohexane Derivatives



Ethyl 2-[(2-Cyanoethoxy)-(4,4-diphenylcyclohexyloxy)-phosphoryloxy]acetate
100mg / 500mg
[E1268]



Ethyl 6-[(2-Cyanoethoxy)-(4,4-diphenylcyclohexyloxy)-phosphoryloxy]hexanoate
100mg / 500mg
[E1313]



4,4-Diphenylcyclohexanol
1g / 5g
[D4973]

Applications

- 1) MS-325: albumin-targeted contrast agent for MR angiography
R. B. Lauffer *et al.*, *Radiology* **1998**, 207, 529.
- 2) The Effect of a Phosphodiester Linking Group on Albumin Binding, Blood Half-Life, and Relaxivity of Intravascular Diethylenetriaminepentaacetate Aquo Gadolinium(III) MRI Contrast Agents
T. J. McMurry *et al.*, *J. Med. Chem.* **2000**, 45, 3465.
- 3) Phosphate ester serum albumin affinity tags greatly improve peptide half-life *in vivo*
K. Zobel, M. F. T. Koehler, *et al.*, *Bioorg. Med. Chem. Lett.* **2003**, 13, 1513.
- 4) Conjugation to albumin-binding molecule tags as a strategy to improve both efficacy and pharmacokinetic properties of the complement inhibitor compstatin
J. D. Lambris *et al.*, *ChemMedChem* **2014**, 9, 2223.

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